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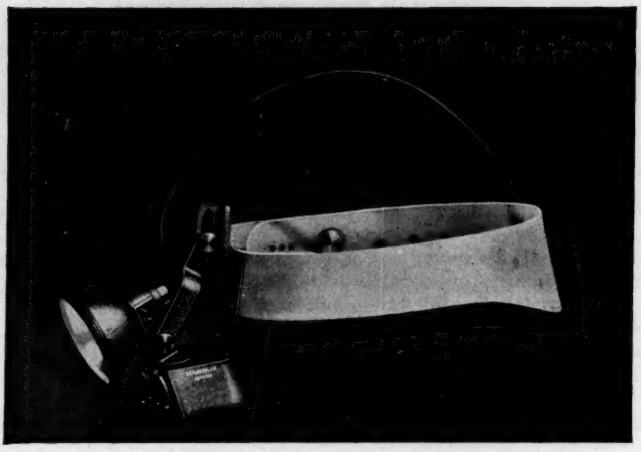

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SIR JOHN PARSONS

Brit. J. Ophthal. (1957) **41**, 705.

OBITUARY

SIR JOHN HERBERT PARSONS

(1868–1957)

The death of Sir John Herbert Parsons, C.B.E., D.Sc., LL.D., F.R.C.S., F.R.S., on October 7, 1957, in his 90th year, at University College Hospital, London, marks the end of an epoch in the story of British ophthalmology. One of the band of great clinical leaders who retained for ophthalmology in this country at the end of the last and the beginning of the present century the proud position in the world it had inherited fifty years previously from Sir William Bowman—Nettleship, Doyne, Gunn, Collins, Fisher, Lawford, Paton, and others—he outstripped them all in intellectual brilliance and force of character. Moreover, unlike them, he grasped the significance of the changes which at that time were apparent in the advance of medicine. Alone among them he realized that advances in ophthalmology did not lie solely in the clinic or in the pathological laboratory, that a new age was emerging wherein clinical pictures were to be interpreted in terms of physiology, physics, and chemistry; and he had the energy and ability to follow out his convictions. Greater as an original scientific thinker and philosopher than as a clinician, he dominated British ophthalmology in the lean and difficult years between the wars, striving to cherish and maintain the spirit of research and succeeding by his personal example, his forceful personality and his transparent integrity. After the war his purpose was achieved when he formally opened the Institute of Ophthalmology in London. And in the long evening of his life the frustrations of physical disabilities, strange to a nature so forceful as his, were softened by the realization that those of a newer generation, whom he had encouraged and nurtured with such paternal care and at the same time without hypocrisy or pretence, were succeeding in establishing his ideals.

Parsons was born in Bristol on September 3, 1868. His education was commenced at the University College, Bristol, aided by his winning successively the Gilchrist, John Stewart, and Sharpey Scholarships and the first entrance scholarship to the Bristol Royal Infirmary; it was completed at St. Bartholomew's Hospital, London. In 1890 he took his B.Sc. degree with honours in physiology, and in 1892 he qualified in medicine. Thereafter he became assistant in the Department of Physiology at University College, and for some years engaged in general practice in the London suburb of Finchley. But, through physiology, his interests concentrated progressively on ophthalmology and he became a clinical assistant at Moorfields Eye Hospital. In 1900 he took his M.B. London and the F.R.C.S. England, and, aided by a British Medical Association Research scholarship, gave up general practice and threw himself into the whole-time pursuit of ophthalmology in its widest aspects with a determination of purpose and brilliance in achievement rarely equalled. Successively clinical assistant, curator and

librarian at Moorfields, he was elected to the surgical staff of that hospital in 1904; he became ophthalmic surgeon to University College Hospital and for a time was ophthalmic surgeon to The Hospital for Sick Children, Great Ormond Street. To the first two of these hospitals he devoted his energies all his working life, retaining a close interest in their affairs after he had retired from their staffs on account of age and had joined their consulting staffs. Along with these duties went the responsibilities of a large consultant private practice.

But it was not in hospital activities nor in practice that Parsons's heart lay; to him practice was not a first love and he was a good but not a brilliant surgeon. He lived for research and the progress of knowledge, at first by contributing lavishly to it himself, later by integrating it philosophically and encouraging its pursuit by others. To such a purpose his unusually wide erudition, the profoundness of his intellect, and his obvious honesty made him eminently suited. To him clinical ophthalmology was insufficient; he must correlate it with all the workings of the visual apparatus—its optics, its physiology, its neurology, and its psychology; he saw the working of the eye in terms of physics and chemistry, of vision in terms of biology. Physiology and optics were his first loves, particularly the control of the intra-ocular pressure; there followed fundamental researches on neurology, particularly the innervation of the pupil; in ophthalmic pathology he became a world authority; and in his later years, through the avenue of colour vision, he devoted most of his energies to the perceptual and psychological aspects of vision and sensory perception in their widest sense.

Out of these activities a vast stream of papers flowed from his pen—he made some 140 contributions to the *Transactions of the Ophthalmological Society of the United Kingdom* alone. In addition there were several books. The first four were relatively small—*Elementary Ophthalmic Optics* (1901), *The Ocular Circulation* (1903), and two translations from German works—Boldt's *Trachoma* (1904) and von Hanke's *Treatment of Diseases of the Eye* (1905). His most popular work, which maintained an immense circulation all through his working life, was his *Diseases of the Eye*, an excellent, comprehensive and uniquely compact manual for students and practitioners which first appeared in 1907 and continually demanded new editions. But his first classical work was his monumental treatise, *The Pathology of the Eye*, which appeared in four volumes (1904–8). As curator at Moorfields he had grounded himself well in pathology, and in this great work ophthalmic pathology was for the first time integrated into a self-contained discipline. The book, for its time, was superb, and through it Parsons established himself in a unique position and became recognized as a world authority. His second classical work appeared in 1915—*An Introduction to the Study of Colour Vision*. Herein he served a great scientific need by presenting in a factual way a vast and difficult subject which hitherto had been obscured by numberless nebulous theories, through the thickets of which he hacked with uncompromising criticism. His later interest in psychology was ushered in by a small book, *Mind and the Nation; a Study in Applied Psychology* (1918). This was followed by the greatest book he ever wrote—*An Introduction to the Theory of Perception* (1927), wherein were expounded his

views on the evolutionary development of the neurology and psychology of perception as applied to all the senses throughout the animal kingdom. It was an immense contribution to science in a field of knowledge muddled by psychological concepts and so wide that its integration could be attempted only by one of outstanding learning and critical capacity. This was followed in his later years by a small monograph—*The Springs of Conduct* (1950)—in which were summarized his neuro-psychological theories with their firm biological basis.

Recognition for this scientific output, vast in scope and profound in content, was ample. We have already noted his student scholarships and B.M.A. research scholarship on the financial aid from which his early progress was dependent. In 1904 he received the Middlemore Prize; and again in 1914. In 1907 he received the Nettleship Gold Medal for his pathological researches. In 1919 he received the Doyne Medal at Oxford; in 1925 he delivered the Bowman Lecture on the "Foundation of Vision"; in 1929 he was invited to assist in the opening of the Wilmer Institute of the Johns Hopkins University; in 1936, going to America again as the guest of the American Academy of Ophthalmology and Otolaryngology, he was presented with the Lucien Howe Medal of the American Ophthalmological Society. He received the honorary degree of D.Sc. from Bristol University, that of LL.D. from Edinburgh; and his scientific achievements were crowned by his election as a Fellow of the Royal Society in 1921.

In addition to these scientific pursuits, Parsons spent much energy in public activities. He joined the Ophthalmological Society of the United Kingdom in 1900 and remained one of its greatest supporters until age and deafness precluded his active participation in its work; in 1925 he was its president. Successively secretary and vice-president of the Section of Ophthalmology of the B.M.A., he was president in 1923, and again in its centenary year, 1932. He performed the responsible task of being chairman of the Editorial Committee of this Journal for 22 years, from its foundation in 1917 to 1948. He was the only ophthalmologist to become president of the Royal Society of Medicine (1936–8). He was one of the founder-members of the British Council of Ophthalmologists, remained as its moving spirit, and was largely responsible for its dissolution and the creation in its place of the Faculty of Ophthalmologists. Moreover, in the field of international ophthalmology, he played a prominent part and was one of the small band of men who succeeded at Scheveningen, in 1927, in re-establishing the continuity of International Congresses of Ophthalmology which had lapsed since the outbreak of the first World War.

In addition he was constantly and intensely active in numerous committees of national importance. He was a member of the Glass-workers' Cataract Committee set up by the Royal Society (1906), of the Departmental Committee on Sight Tests set up by the Board of Trade (1910), of the Home Office Committee on Factory Lighting (1913), of the Committee on Eyestrain in Cinemas of the Illuminating Engineering Society (1919), of the Committee on the Causes and Prevention of Blindness set up by the Ministry of Health (1920), and on the B.M.A. Special Committees on Tests for Motor Drivers (1929–31) and on Miners' Nystagmus (1935–6; 1938–40). On all

of these subjects he spoke with authority. In the first World War, with the rank of Colonel, he was appointed Ophthalmic Consultant to the home forces. In 1919 he joined the Advisory Medical Council of the Air Ministry; in 1922 of the Admiralty. Just before the second World War he became civil consultant to the Royal Air Force, and shortly thereafter joined the Flying Personnel Committee which concerned itself with all matters affecting the safety and efficiency of the R.A.F. For these public works as well as for his scientific eminence he was created C.B.E. in 1919 and knighted in 1922.

Of the greatest importance to ophthalmology, however, was his participation in the work of the Medical Research Council on which he served from 1928 to 1932. A close friend of its first Secretary, Sir Walter Fletcher, and for long the chairman of its Committee on Vision, he bent all his powerful influence to stress the scientific and national importance of research in visual problems; and he succeeded. It was due to his efforts and his encouragement that a nucleus of research was kept alive in this country in the years between the wars, for it was he who was responsible for the provision of opportunities and funds for original work for such men and women as Lythgoe, Craig, Katharine Tansley, Ida Mann, Dorothy Campbell, and myself, when these would otherwise have been completely lacking.

This was indeed a full life and a magnificent record. How about Parsons, the man? Perhaps I am the wrong person to write about this; because I loved him—even for his apparent harshness, his ruggedness and cynicism, as well as for his kindliness, his fatherliness, and his unfailing loyalty. To him I owe everything; he taught me ophthalmology and made possible anything I may have done professionally. He was indeed a great man, massive in physique and mind, inexhaustible in his capacity for work, and rock-like in his intellectual honesty. To me this last was his most striking characteristic; pretence, compromises, or placation had no place in his make-up. A shrewd judge of human character, he was no respecter of persons, and he said what he thought without hesitation—often with a wit so mordant as to be devastating. Yet this exterior clothed a nature that was essentially modest and shy; and because he lived largely alone, he appreciated friendliness which was sometimes lacking to him because by nature he tended to stand aloof and detached. Rarely has so great an intellectual ability, a profundity of philosophical thought, and a force of character been combined with a disposition so loyal and fundamentally affectionate.

It is good that all these qualities were recognized in his lifetime by his colleagues. His happiest day, he said, was on the occasion of his 80th birthday, in 1948, when he was presented with his portrait by his colleagues as represented by the Ophthalmological Society and the Faculty of Ophthalmologists—a portrait which now hangs in the Institute of Ophthalmology. He was immensely proud, too, of the special number of this Journal which was published at the same time in his honour. We need have no regrets at his death, for his life was long, splendid, and full; in his later years he saw the realization of most of the things he cherished and for which he fought. Therein he was, I think, content. It is not always so. And the end was peaceful and to him not unwelcome.

STEWART DUKE-ELDER

Brit. J. Ophthal. (1957) **41**, 709.

COMMUNICATIONS

STEREOSCOPIC VISION*

I. EFFECT OF BINOCULAR TEMPORAL SUMMATION

BY

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UNTIL 1926 it was believed that stereoscopic vision required the simultaneous function of both eyes. Two simultaneous disparate retinal images were thought necessary to produce a synchronous discharge in the optic nerves before a sense of depth could be achieved. Langlands (1929), in his study of binocular depth acuity, showed that both eyes need not observe the scene simultaneously, provided that they viewed it alternately. With a sufficiently high rate of alternation of the "viewings" by the left and the right eyes a sense of depth could still be realized. Langlands did not study the time relationships between these alternate viewings in any detail as he was more interested in a quantitative analysis of the limits of stereoscopic visual acuity. The phenomenon of stereoscopy with alternate "viewings" has been studied by Pi Suñer (1947).

In the course of the present experiment, which was primarily designed to demonstrate a "scanning mechanism" within the occipital cortex, Langland's studies were repeated and greatly extended. The results of these experiments, though not confirming the existence of a scanning mechanism, did reveal a form of temporal summation within the visual system which had not been previously studied.

The present experiment was designed to study "stereoscopic vision" but not "visual depth perception". The difference between these two terms is profound. Visual perception of depth is determined by a large number of sensory and psychological factors. The least significant of these, from a practical point of view, is binocular stereoscopy.

The other factors which are chiefly responsible for the sense of depth have been studied in great detail by Riddoch (1917), Neff (1936), Pi Suñer (1947), and Vernon (1952), and do not concern us here, except in so far as they have been specifically eliminated from the experimental setting. They are based in large part on the psychological assumption that the object casting the largest retinal image will appear to be the closest to the subject. This instinctive assumption is rapidly and unconsciously modified if there is any previous information concerning the absolute size, shape, colour, or surface features of the object.

* Received for publication March 11, 1957.
† Fellow of The National Foundation For Infantile Paralysis (U.S.A.).

All these psychosensory reservations which modify this basic assumption stem from sensory data which can be perceived by one eye alone. Hence they have been called "monocular clues to depth perception". These monocular clues account for most of the accuracy of depth discrimination at distances greater than 18 metres and explain very well why one-eyed people have so little difficulty in depth discrimination. They also explain why such people never complain that the world looks "flat". One subject (Riddoch, 1917) complained that his world was peopled with "pasteboard" models which did not appear to displace any volume. Such cases are due to cerebral lesions which have damaged those parts of the occipital lobes which, in normal people, apparently integrate all the monocular clues of perspective into a "sense of depth".

For distances under 18 metres, binocular factors begin to come into operation and are progressively more significant in producing a sense of depth as the distance from the object to the eyes becomes smaller. These binocular factors consist of convergence, accommodation, proprioceptive data from the extra-ocular muscles, and true disparity of retinal images. The first three factors play a small role and can be neglected in most experimental situations. Even when combined, they play such a small part in stereoscopy when compared with the effect of retinal disparities that for our purposes it is not important to consider them further.

In the present study, all the monocular clues have been assiduously eliminated, as have all binocular clues, except for the difference in parallax produced by looking at an object from two different positions. In other words, this experiment was designed to study that function of the brain which is concerned with recording and integrating a series of parallactic differences (retinal disparities) to create an illusion of depth.

Apparatus

The basic form of this experiment is that of alternating exposures of each eye to a scene which, when viewed simultaneously by both eyes, would produce a marked sense of depth. The variables of this visual stimulation are:

(1) The time between the end of the stimulus to the first eye and the start of the stimulus to the second eye (this will hereafter be known as the SHORT INTERVAL).

(2) The time between the end of the stimulus in the second eye and the start of the stimulus to the first eye again (this will be known as the LONG INTERVAL).

(3) The time allowed for each eye to view the scene (this will be called the FLASH DURATION).

(4) The intensity of the flash exposure for each eye measured not in actual physical units but rather on an arbitrary scale.

(5) The shape of the curve of each light impulse, the axes of this curve being light intensity *versus* time. It might have been, for example, a slowly rising intensity curve, a rapidly decaying curve, etc. An almost square wave impulse was used mainly for convenience in timing the onset and the termination of the pulse.

An all-electronic system would have ensured the absolute control of these independent variables. A simple mechanical system, however, was used in this pilot experiment. In it at least two variables were always linked together. But the final mathematical analysis of the independent effect of each variable was far simpler than anticipated. Some of the linked variables proved to have little effect on the outcome, and a complete analysis of the precise quantitative relationships between all the variables was thus not undertaken. The results printed here are specifically limited to the outstanding characteristics of the phenomenon studied.

(1) Visual Scene.—The subject was required to look into an ordinary "three-dimensional" viewer consisting of two independent optical channels. For each eye there was a simple convex lens which served as an eyepice and produced a moderately magnified image. When the observer looked into the viewer with both eyes, he saw only a single square background of ground glass illuminated from behind. A photographic plate, consisting of two almost identical images on a black-and-white transparency, was placed between the eyepieces and the ground glass. One image was on the left side of the rectangular plate, and was photographed with the left half of a stereo camera. The right side of the plate was the same scene photographed by the right half of the same camera.

With each eye the subject saw three black letters of exactly the same size and density (totally opaque) against a featureless white background. If he looked with either eye *alone* the three letters appeared to be on one plane and all equidistant from the observer. There was no indication whatsoever that one of these letters was "closer" than another. On the other hand, when the subject looked with both eyes simultaneously and under continuous illumination, it became clear that each letter was at a different distance. A sense of depth was created in this fashion which was uncontaminated by monocular clues or by other psychological inferences.

By using the optical formula $\frac{\text{Object Size}}{\text{Image Size}} = \frac{\text{Object Distance}}{\text{Image Distance}}$, it was possible to construct letters of three different sizes, which, when suspended at appropriately calculated distances from the camera lenses, nevertheless cast the same-sized image on the plate (Fig. 1).

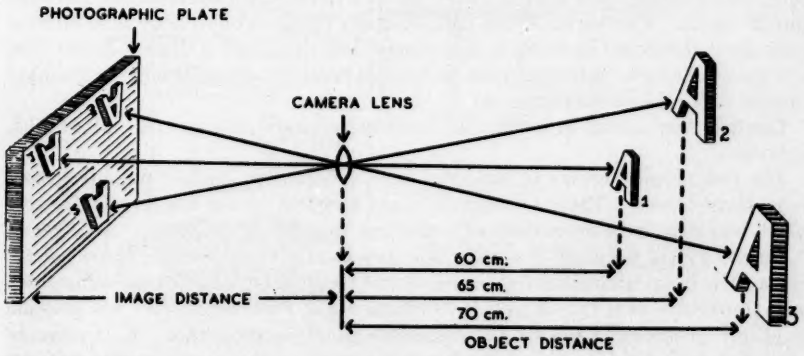

FIG. 1.—Method of photographing three objects (A1, A2, A3) so that images are of identical size on plate.

The three A's were photographed so that the first letter was 60 cm. from the camera lens, the second 65 cm., and the third 70 cm. By adjusting the size of the letters (without altering the case or the shape) all produced images identical in every respect on the photographic plate.

One hundred such slides were made with random combinations of three letters arranged to lie at the apices of an equilateral triangle. On one-third of the slides the letter at the left base was actually the nearest, on one-third the letter at the right base was the nearest, and on the last third the letter at the apex was the nearest. These slides were presented to the subject at random.

One such slide is reproduced in full size (Fig. 2). When it is viewed with the convex lenses, the letters appear much larger, occupying about 20° of the central visual field, and the whole field is filled by the slide.

FIG. 2.—Full-scale reproduction of stereoscopic transparency. Note absence of all monocular clues to three-dimensional arrangement.

The only information contained in this pair of images is:

(*a*) The alphabetical identity of the letters themselves.
(*b*) The triangular relationship of the three letters.
(*c*) The parallactic differences between the two sides of the slide.

It is with this last alone that we are concerned.

(2) Optical System.—The light source was a 6-volt, 36-watt automobile headlight bulb, with a linear, thick filament, supplied by a transformer operating on 220 volts and 50 cycles. The variations in light intensity produced by the cyclical alternations are insignificant in terms of this experiment, since such a thick filament does not cool sufficiently between cycles to alter appreciably the character of the light emitted. No flicker was observed.

The light was placed in a box with condensing lenses at opposite ends (Fig. 3, opposite).

The two parallel beams so produced were reflected by mirrors directly to two short-focus lenses. These formed an image one-fifth of the size of the filament which was cast upon the surface of a rotating sectored disk.

On theoretical grounds, it is clear that any focal plane shutter operating at the focus of a point source of light will permit the full intensity to be transmitted instantaneously as it moves past the dimensionless point-focus, and will also cut it off instantaneously. This dimensionless point-focus cannot, of course, be produced with real lenses, and the actual thickness of the images in this case was 0·5 mm. The calculated time before full intensity was reached (the so-called

"rise time") was less than 0·2 msec., while the total duration of the flash could be varied from 3 to 80 msec.

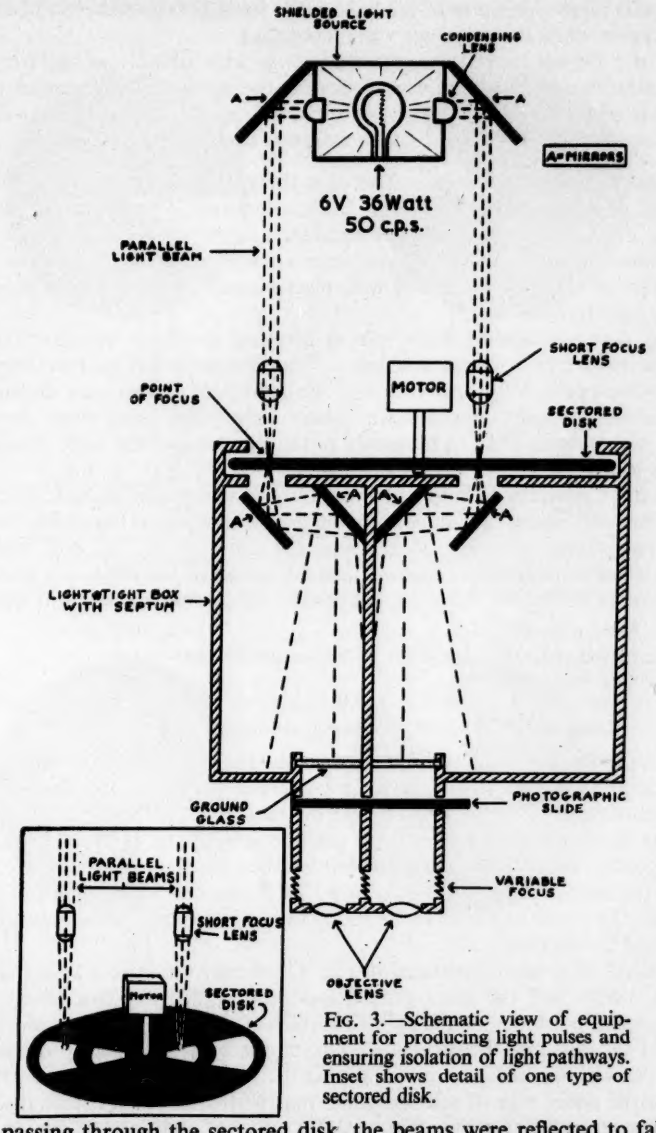

FIG. 3.—Schematic view of equipment for producing light pulses and ensuring isolation of light pathways. Inset shows detail of one type of sectored disk.

After passing through the sectored disk, the beams were reflected to fall upon the right and left surfaces respectively of the ground glass of the three-dimensional viewer. These features of the optical system are illustrated in Fig. 3, which also

shows that the separate light pathways were of identical length, thus producing equally bright illumination for each eye. Inspection of the figure will also reveal that this complete separation of the light paths could permit one eye to be kept in total darkness while the other eye was illuminated.

When the subject looked through the viewer with suitable prisms for proper convergence, one large square was observed—the result of the fusion of the two monocular squares. The light was of such an intensity that the eyes were light adapted at all times. Artificial pupils were not considered necessary.

(3) **Mechanical Timing System.**—The disk through which the light passed was composed of a transparent plastic 14″ in diameter and ¼″ thick. It was centrally mounted on a thyratron-controlled constant speed motor. The motor speeds were calibrated stroboscopically and were controlled by a Wheatstone bridge. The surface of the disk was coated with black enamel paint except for those areas used for light transmission.

In Fig. 4(*a*) two opaque disks spin at identical speeds in the same direction. A transparent sector is left in each disk. When the sectors of the two disks finally rotate to the position illustrated in Fig. 4(*a*), the light beams pass through both sectors simultaneously, producing a square light pulse once every revolution. The left disk permits light to pass only to the left eye and the right disk only to the right eye.

If the disks continue to spin as before, but the two beams of light are lowered so that they fall below the line joining the axes of the disks (Fig. 4(*b*)), the pulses are no longer synchronous. The transparent sector of the left disk reaches the focal point of its light beam sooner than the sector of the right disk reaches the focal point of its beam. With the light beam lowered the subject will receive:

(*a*) a flash in the left eye;
(*b*) a period of total darkness for both eyes (SHORT INTERVAL);
(*c*) a flash in the right eye,
(*d*) an even longer dark interval for both eyes (LONG INTERVAL) before the next couplet of flashes occurs on the subsequent revolution.

This is illustrated by the time scale at the base of Fig. 4(*b*).

The duration of either of the two dark intervals in milliseconds will depend on the speed of rotation of the disk and the distance by which the focal-points of the light beams have been lowered from the line joining the centres of both disks. If the speed is held constant, the interval between the flash in the left eye and the flash in the right eye (Short Interval or S.I.) will increase as the beams of light are lowered. This will continue to be the case until the light beams are no longer intersected by the disk.

Two disks have been illustrated in Fig. 4, but only one disk was actually used (Fig. 5), which had the same geometrical properties. The two beams of light were brought to a focus on the painted surface of the disk: one at 6 cm. from the centre of the disk and the other at 14 cm. on the other side of the centre. Two series of concentric sectors were cut, so that the left-hand light beam always passed through the outer ring of sectors, while the right-hand beam passed through the inner ring of sectors (see Figs 5(*a*) and 5(*b*), overleaf, and inset in Fig. 3).

It is obvious that it makes no difference whether the light beams are moved and the disks are held fixed, or *vice versa*. In the experiment, the light beams were

held fixed and the thyratron-controlled motor on which the disk was spinning was raised or lowered with the aid of a lathe component called a "vertical rise". Great accuracy could be achieved in the movements of the disk. Figs 4 and 5

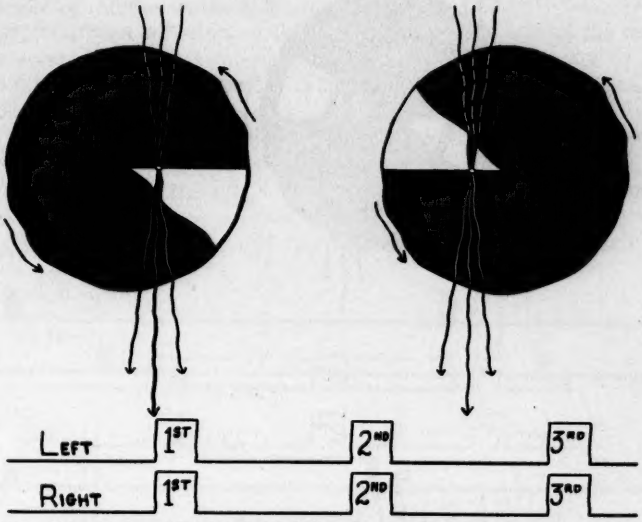

FIG. 4(*a*).—Beam of light brought to focus on line joining centre of two disks. At the moment, a square pulse of light is just beginning. Note that pulses are synchronous. The disks spin at identical speeds and in a fixed phase.

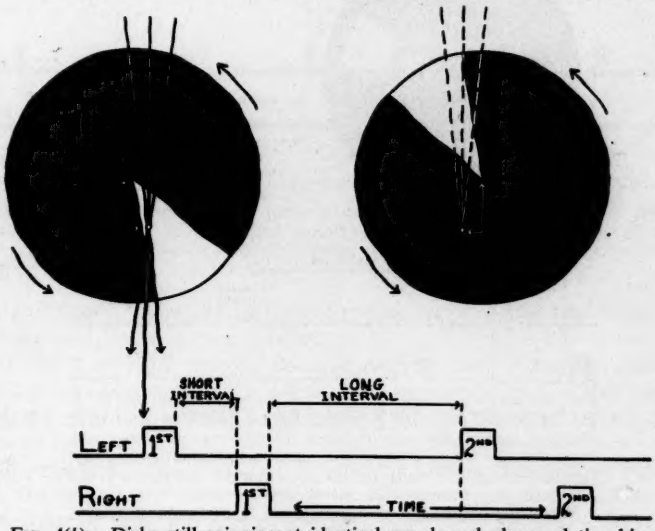

FIG. 4(*b*).—Disks still spinning at identical speeds and phase relationships unchanged. Here the two beams of light strike the disk *below* the line joining the centres, and the light pulses are no longer synchronous.

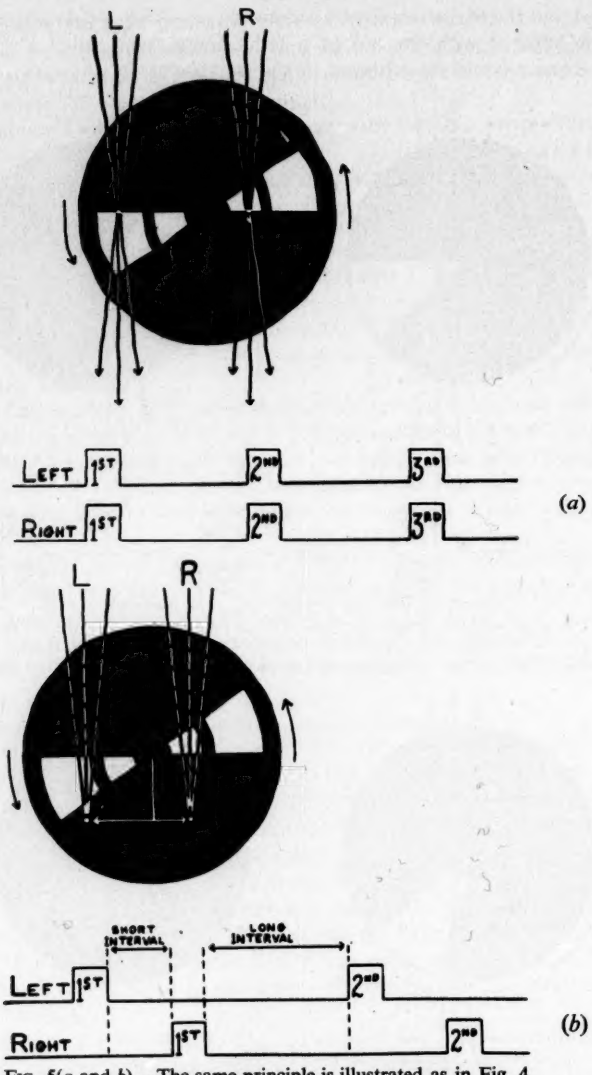

FIG. 5(*a* and *b*).—The same principle is illustrated as in Fig. 4, but here only one disk is used. By utilizing two concentric rings of sectors the same control of light pulses is achieved. Note that the beam ultimately destined for the left eye always passes through the outer set of sectors, while the beam to the right eye always passes through the inner sectors.

When the two beams are on the same line as the disk centre, the light pulses are synchronous (Fig. 5(*a*)), but when the light beams are lowered asynchrony results.

Note: Pulse duration controlled by varying sector width (not shown in diagram).

show that any movement of the disk will alter the ratio between the Long Interval and the Short Interval. The absolute time interval of these two periods in milliseconds (for any given position of the disk relative to the beams) is determined by the speed of rotation of the disk.

The procedure actually used in this experiment was to pre-set the ratio of the Long Interval to the Short Interval (L.I./S.I.) by placing the disk in a definite position relative to the light beams. The subject was then permitted to look into the eyepieces. The motor was slowly accelerated until the end-point was reached. (The nature of the end-point will be discussed below.) The actual alteration in the nature of the stimulation, as the motor was accelerated, is illustrated in Fig. 6, which shows the pre-set ratio L.I./S.I. of 4·0. As the motor was slowly accelerated, the ratio determined by the position of the disk remained constant. What did change, however, were the short interval, long interval, and flash duration measured in milliseconds.

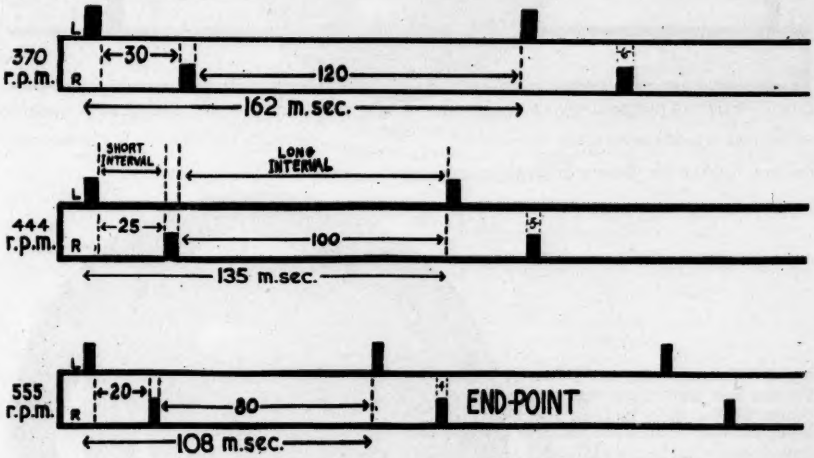

FIG. 6.—A pre-set ratio $\left(\frac{\text{long interval}}{\text{short interval}}\right)$ of 4·0 was selected. The disk is accelerated gradually from 370 to 555 r.p.m. Although the ratio is constant, the absolute duration of the intervals has shortened. The duration of the light pulse changed from 6 to 4 msec. The short interval has been reduced from 30 to 20 msec. at 555 r.p.m. The stereoscopic end-point was reached (see text).

Fig. 7 (overleaf) illustrates a number of pre-set ratios. A large number of such ratios were used, varying from 1 to 80.

Fig. 6 shows that the variable of flash duration was not under independent control. It was impossible to know *a priori* the significance of this variable in affecting the results. A new arrangement had to be devised to make the flash duration as independent a variable as possible. Two new disks were made and were superimposed. One disk carried only the sectors transmitting light to the left eye, the other only those transmitting light to the right eye. These superimposed disks are shown in Fig. 8 (overleaf).

In these conditions, it will be apparent that *rotation* of one disk relative to the other alters the ratio L.I./S.I. The ratio once set was held fixed by clamping the two

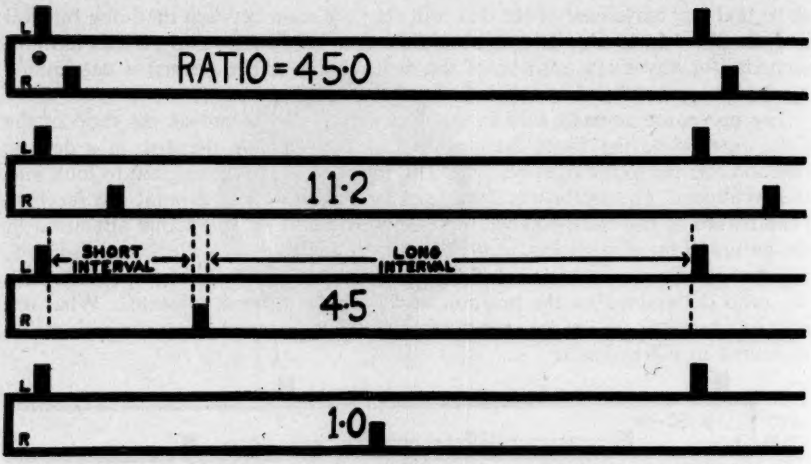

FIG. 7.—Effect of progressively lowering beams of light below axis of disk. The speed of rotation of the disk is held constant, but the ratio $\left(\frac{\text{long interval}}{\text{short interval}}\right)$ is gradually decreased. In this example the sum total of the various intervals is unchanged.

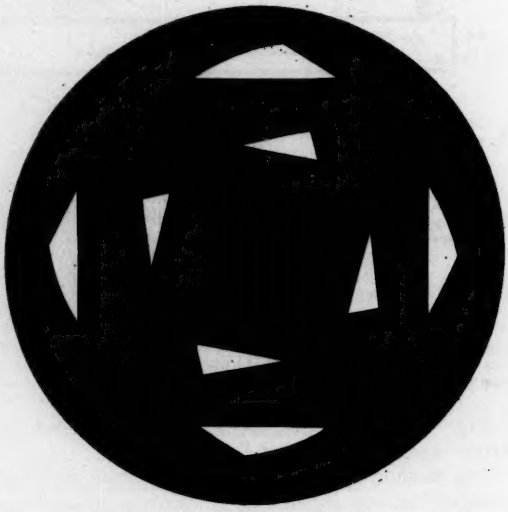

FIG. 8.—Two superimposed disks. On one four sectors are near the centre of the disk, and on the other the four sectors are nearer the periphery. The ratio L.I./S.I. was altered by turning one disk relative to the other. After a given ratio had been selected, the two disks were clamped together.

disks together. The sectors were so shaped that raising or lowering the disks on the vertical rise produced a variation, not in the timing of the two pulses, but rather in the duration of the pulse itself. When the disk was raised or lowered, the arc through which the point-focus of light passed was altered. In the neutral position (Fig. 9(*a*)), the beam of light passed through that part of the sector which was 45° in width. When the disk was raised 5 cm., the sector through which the light passed was only 3° of arc. Various flash durations could be used,

determined by sector widths from 3° to 45° of arc—an increase by a factor of 15. It was still true, however, that, for a given position of the disk relative to the light (*i.e.* for a given sector width), the faster the disk rotated the shorter was the flash

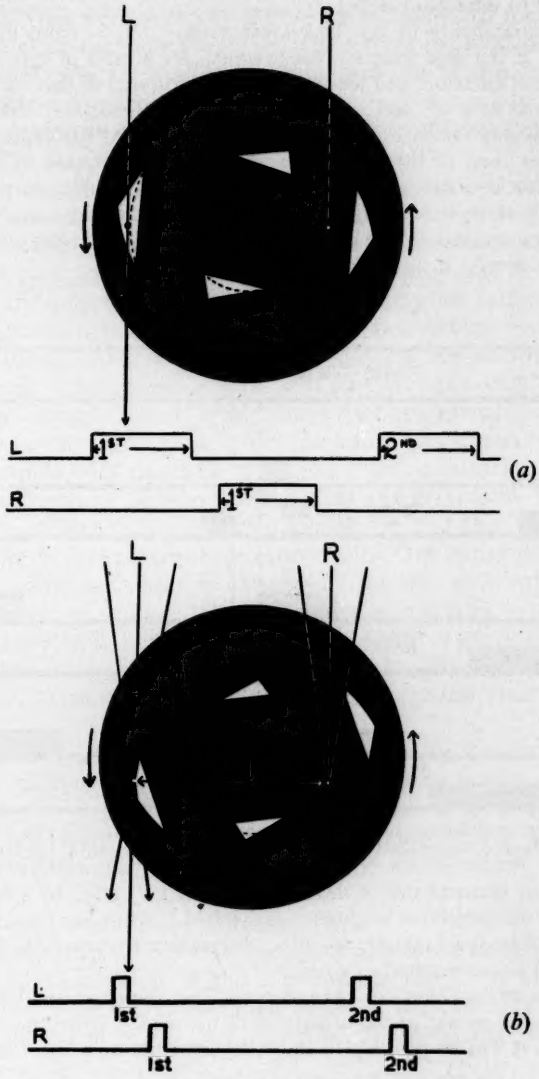

FIG. 9(*a* and *b*).—The same disk as in Fig. 8 (with only two sectors in each ring transmitting). In this geometrical arrangement of sectors, lowering the light beams reduced the duration of the pulse and the ratio L.I./S.I.

duration. The results will indicate that this small change in flash duration produced during the acceleration of the disk, even when under maximum control, did not alter to any significant extent the variations in the end-point, which were due far more to the ratio L.I./S.I.

Another consequence of this disk arrangement follows from the geometry of the sectors. If the disk were set, for example, for a ratio of L.I./S.I. of 3·96 for a 3° sector flash duration, and the disk were then lowered so that the flash duration was determined by a 45° sector, the ratio L.I./S.I. fell to 1·57. The sectors were so drawn that any increase in the flash duration was at the expense of the long interval rather than of the short interval. This is illustrated in Fig. 10, which shows the effect of a disk spinning at a constant speed with a starting ratio (for a 3° sector arc) of 10·4, and a gradual alteration of this ratio to 2·0 as the flash duration was increased. This occurred *despite* the fact that the disk was rotating at a constant speed.

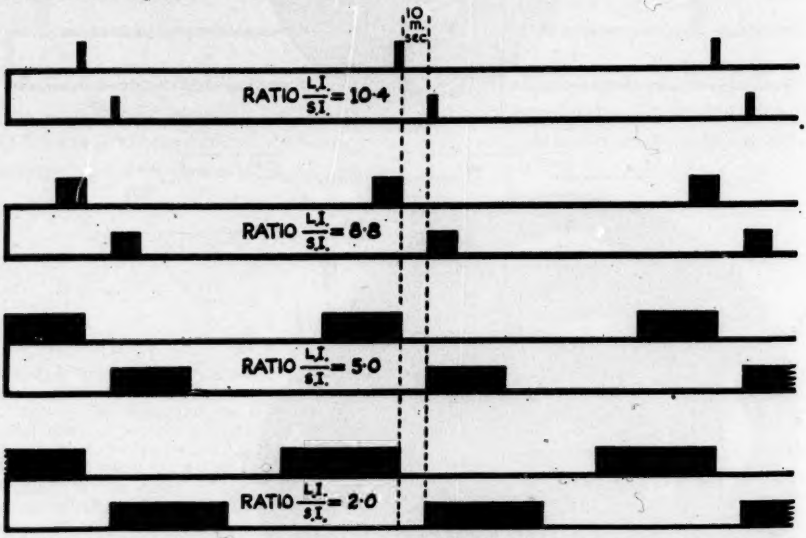

FIG. 10.—Effects of changing pulse duration by using the disk shown in Figs 8 and 9. Not only was the pulse duration lengthened (from top to bottom) but the ratio L.I./S.I. was also changed.

Still another consequence of this change in flash duration by a factor of 15 was the effect on the subjective brightness of the field. At flicker fusion the brightness is determined by the Light-Dark ratio. Increasing the number of sectors or the width of any sector resulted in a brighter field at the flicker fusion frequency.

It can thus be seen that any change in the flash duration simultaneously altered the ratio L.I./S.I. as well as the brightness of the field. When the objective results are graphed, it will be possible to show the influence of each of these variations.

The Subjects

The subjects were instructed to look into the viewer; they were told that the three letters would appear to lie in the same plane, but that they would

eventually emerge from the featureless background, and would then appear to lie on three different planes. They were also instructed to pay no attention to flickering illumination or to any horizontal movement (phi phenomenon) of the letters. They were to report at once the moment that they could with *certainty* distinguish the sequence of the letters from the most distant to the closest. A good observer would learn this technique after a few trials and would thereafter report the end-point in a precise and reproducible fashion without ever making an error. The "scatter" from one test slide to another was very small with a "good" subject.

Unfortunately only 30 per cent. of the available subjects could be considered good ones for this experiment. A number of possible candidates had non-correctable visual defects in one or both eyes which precluded any stereoscopic vision. Other subjects had normal vision but were unable to see much depth using the stereoscope, even in the usual fashion with continuous illumination in both eyes. (This particular defect has been mentioned in previous studies on stereoscopic vision, but the reason for the failure remains obscure.) Still other subjects said that they saw depth clearly—in some cases providing "normal" quantitative data at appropriate disk speeds —but reported an incorrect sequence of the letters ("reversals"). It would appear that people with this type of response are not usually able to synthesize in their central nervous systems correct perceptions from purely stereoscopic (parallactic) data. Any subject who had this type of defect was not used in the main body of the experiment. One last group of subjects showed appreciable variations in threshold from one moment to another and made occasional errors. There was excessive scatter in their results and they fatigued easily, and for these reasons they were also eliminated. Too many physiological principles have been elucidated by studying the "good" subject alone for this systematic exclusion of the "bad" subject to be questioned.

The results of this experiment are thus restricted to those subjects who performed so reliably on numerous trials over a period of several weeks, that any change in their performance could be related to a change in the experimental conditions. Such subjects were studied under varying conditions of stimulation and showed characteristic results which will now be described.

Results

(A) Subjective Results.—When the subject looked into the viewer he observed two phenomena in addition to the one towards which his attention was formally directed. He was immediately aware of the flickering white background. As the speed of the disk increased, the flickering became faster and finer and finally disappeared.

The second phenomenon was considerably more important, on practical as well as on theoretical grounds. The subject was always startled, at the practice trials, when he observed horizontal movement of the letters. (This

type of movement, which has been known for many years to psychologists and is the very basis of the cinematographic effect, has been termed the "phi phenomenon".) The whole subject has been reviewed in exhaustive detail by Neff (1936) and Vernon (1952). The slower the rate of intermittence of the light, the coarser (larger) the apparent horizontal movement. As the disk accelerated this movement became a finer oscillation from side to side, and became smoother.

This apparent horizontal movement is related to the flickering background, as it is obviously of the same frequency as the flicker. When the threshold of stereoscopy was approached, the horizontal oscillatory movement was quite small, and did not prevent the subject from observing the end-point—a phenomenon quite distinct from the movement. For some subjects the apparent movement was still present to a moderate degree when they could see the scene in depth, but for others, including the author, the phi phenomenon had long since disappeared when the letters slowly began to place themselves at different depths. Similarly, the presence or absence of flicker was independent of the end-point.

The first phenomenon of stereoscopy took the following form:

The letters began to oscillate forward and backward in the plane perpendicular to the photographic slide. This movement was at right angles to the phi phenomenon and was qualitatively unlike it. For a second or two, one letter was closer to the subject than another, and just a moment later, it seemed to recede slowly into the background. It did not jerk back and forth with the frequency or the speed of the flicker, as did the phi phenomenon. This state of slow to-and-fro movements of the letters could be prolonged indefinitely by keeping the disk running at the same speed. The subjects began to sense a depth phenomenon, but could not yet, with certainty, list the sequence of the letters, which constantly changed in their relative positions. This state was probably the physiological end-point.

It was necessary, for a reliable determination, to run the disk just a bit faster. When this was done, the to-and-fro movements ceased and the letters slowly began to move towards the subject. The letter which was destined to be the closest moved out from the plane of the background earliest, and could be distinguished as the "closest". Almost every subject stated that he was sure which letter would turn out to be the nearest, because this was the first one that moved forward quite markedly at this stage. When this happened the proper position of the remaining two was still in doubt, the closest letter stimulating the retinal points which are more disparate than the retinal points stimulated by the "farthest" letter (when the visual axes are parallel).* But as the disk was slowly accelerated, the second, or middle, letter emerged from the background upon which the third, or

* An analogy can be drawn at this point to a "two-point discrimination test" used clinically in neurological practice. In this analogy, the two retinal points can be compared to the cutaneous points of the test. As in all tests for "cortical" sensory thresholds, fluctuations are found in the absolute threshold.

most distant, was still seen. *This* was the end-point used for all the results reported below.

At this stage the subject saw quite clearly that the three letters were all at different distances from him. He insisted that he was correct, and at this stage, could not be persuaded to change his mind. This emergence of the three-dimensional scene was chosen as an end-point because it developed suddenly, was easily recognized, and was psychologically impressive. All new subjects were told that this feeling of sudden, absolute certainty would constitute the end-point.

It is important to note that, when the disk ran still faster, the letters protruded even more markedly from the background, until finally they were as three-dimensional in appearance as they were when the slide was viewed under continuous illumination of both eyes. It was quite difficult to determine the exact point when maximum depth effect was achieved, and for this reason, the obvious stage of abrupt recognition was chosen for the end-point.

It is of considerable psychological interest to note that the subject who once sees a true stereoscopic scene at a given rate of rotation will persist for some time in seeing this scene in depth although the disk is markedly slowed. His threshold for this slide cannot be determined in the reverse direction—from the stage of stereoscopy to its dissolution at slower speeds—since he already "knows the answer". A new slide will give the absolute threshold again. The first slide may be re-used when the subject has forgotten the sequence of letters on it. Thus, with one hundred slides the combinations of letters are so numerous that the subject cannot remember a particular slide for more than a few minutes.

One further psychological effect was noted. When the letters were arranged so that the sequence, as described by the subject, spelled out a word such as D-O-G or M-A-D, the subject tended to see the scene in depth at a significantly lower threshold than if the combination of letters was meaningless. This was a minor factor which was easily corrected. In no case did it ever alter the threshold value by more than 10 per cent. The phenomenon was not studied further.

(B) Objective Results.—Up to this point all the subjective phenomena have been related to the speed of rotation of the sectored disk. We must now translate the r.p.m. of the disk into more meaningful physiological terms.

(1) *Effect of Change of Ratio of L.I./S.I.*—The change in the ratio of L.I./S.I. was the most important variable in determining the maximum permissible time between the flash in the first eye and the flash in the second eye.

Example.—The ratio of L.I./S.I. was set at 2·86, the disk was slowly accelerated until the end-point was reached. At this point the disk was spinning at 163 r.p.m. The calculated S.I. was 46·1 msec., the L.I. was 132 msec., and the calculated flash duration for each eye was 3·07 msec. These values indicate that the S.I.

would be as long as 46·1 msec. with stereoscopic fusion still possible. When a new ratio was chosen (such as 33·9) the S.I. changed; *i.e.* the disk was required to spin at a different speed.

It is clear, therefore, that the S.I. was not a physiological constant but a dependent variable in this experimental situation. The major factor which was varied is the ratio L.I./S.I., and it is this change which produced the alteration in the S.I.

When the S.I. was plotted against the variable ratio L.I./S.I. (Fig. 11), an interesting relationship between these two variables developed, in which they were not only related inversely, but followed, with surprising accuracy, a hyperbolic curve. This was true for *every* subject. Fig. 11 shows this curve for one subject (J. C.) and also the mean value for eleven subjects under identical conditions. This graph indicates that the mean values for all subjects follows the same shaped curve as the curve for an individual subject. With only eleven subjects one cannot, of course, speculate on the normal spread. Nine of the eleven subjects gave results that were within 10 per cent. of each other. Two subjects provided identically-shaped curves, but gave values which were 75 to 100 per cent. higher than the mean of the other nine subjects. The mean values in Fig. 11 include these two subjects and this explains why the curve for the combined values is so far "above" that for the single subject J. C., who was one of the nine "more normal" people.

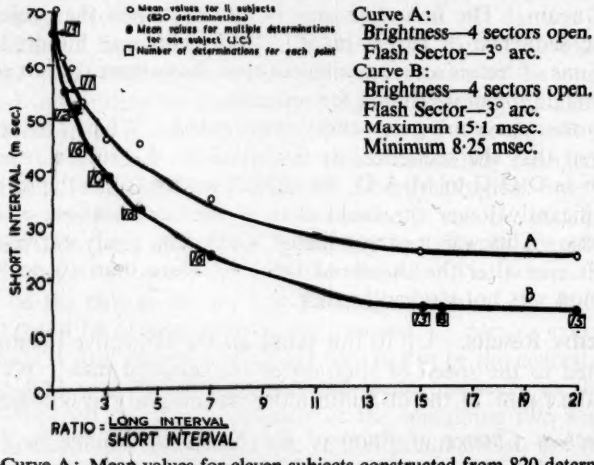

FIG. 11.—Curve A: Mean values for eleven subjects constructed from 820 determinations. Curve B: One subject, number of determinations for each point shown in box.

At this point it can quite definitely be stated that, the longer the interval before the second couplet of flashes, the shorter must be the interval between each of the two flashes of the couplet for stereoscopic vision to result. The curve tapers asymptotically as the ratio L.I./S.I. approaches infinity, sug-

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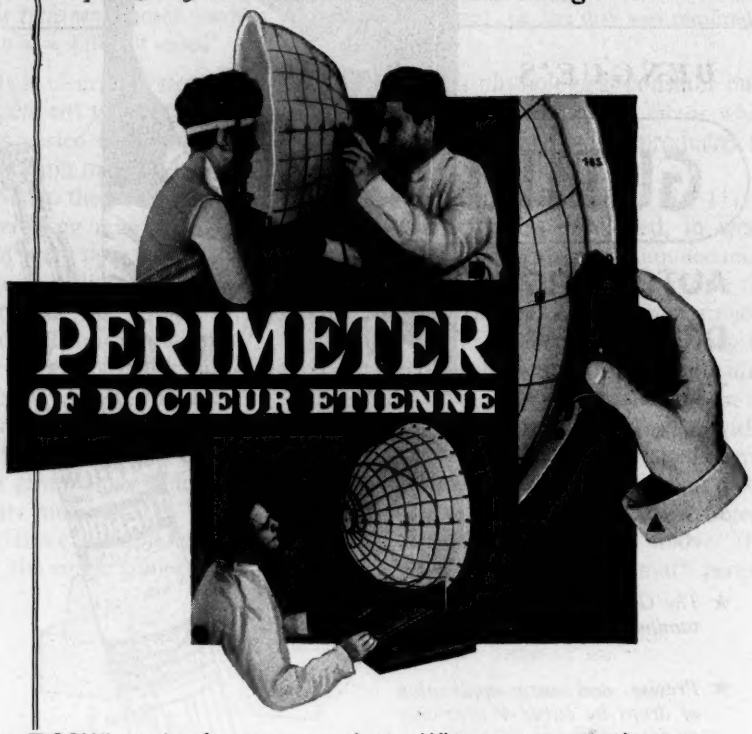

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gesting that a minimum value for the S.I. can be obtained. This minimum value for subject J. C.—with the given illumination conditions—would be about 13 msec. By mathematical extension, if the couplets are separated by an infinite period of time, the component flashes of a given couplet may not be separated by more than 13 msec. for stereoscopic vision to result in this subject.

It must be stated quite explicitly that the use of the revolving disk precluded the production of an isolated couplet. The inference that an absolute minimum value for the S.I. exists for every subject is derived from the shape of this curve. Indeed, this inference is substantiated by Langlands (1929), in whose study just one couplet of flashes in a non-repetitive system was used. He found, in two subjects, that intervals of 25 and 18 msec. between the flashes could still result in stereoscopic vision. If the interval were greater than this, stereoscopy did not result. Langlands used very faint flashes from Leyden jars for his illumination and also used a slightly different type of visual test object in which not every monocular clue was eliminated. While we cannot compare his recorded minimum values with ours, his data confirms our inference concerning the asymptotic nature of the curve and allows us to determine precisely the rate of decay of this temporal summation.

The other end of the curve represents the lowest possible ratio of 1·0. In this case there are no longer any "couplets", but, rather, equal intervals between the flashes (Fig. 7, bottom line). The interval between two flashes may be much longer (up to 182 msec. for one subject) and still permit stereoscopic fusion. This effect of repetition of the stimulus clearly reflects a process of temporal summation within the visual pathways.

The important variable which determined the maximum possible interval between component flashes of a "couplet", and yet allowed stereoscopy to result, was the ratio of L.I./S.I. This ratio is, indeed, nothing more than a reflection of the frequency of couplet repetition. When this ratio is high, we are dealing essentially with a single couplet. There should thus be a definite relationship between the S.I. in milliseconds and the L.I., just as there was a relationship between the S.I. and the ratio L.I./S.I. This was indeed the case, and the shape of this curve, too, was hyperbolic.

It is of some importance to try to locate the region in which this temporal summation is accomplished. Is it a function of retinal "persistence" or does it result from a more central process, perhaps in the visual cortex itself? To answer these questions, at least in part, two other variables must be considered.

(2) *Effect of Brightness.*—The results plotted in Fig. 11 were recorded when all the four possible sectors for each eye were uncovered. The field, as viewed by the subject *after flicker disappeared*, was twice as bright as it would have been if two sectors were open, and four times as bright as it

would have been if only one sector were open. The quantitative results of these various changes in illumination differed, although the same hyperbolic curves were obtained for each level of brightness. This feature is demonstrated in Fig. 12, which shows the differences in the absolute values obtained with three different brightness levels for one subject (E. M.). Inspection of these curves shows that, the brighter the light at any given ratio, the shorter the S.I. *had to be* for stereoscopic fusion (although the difference became progressively less significant as the ratios increase).

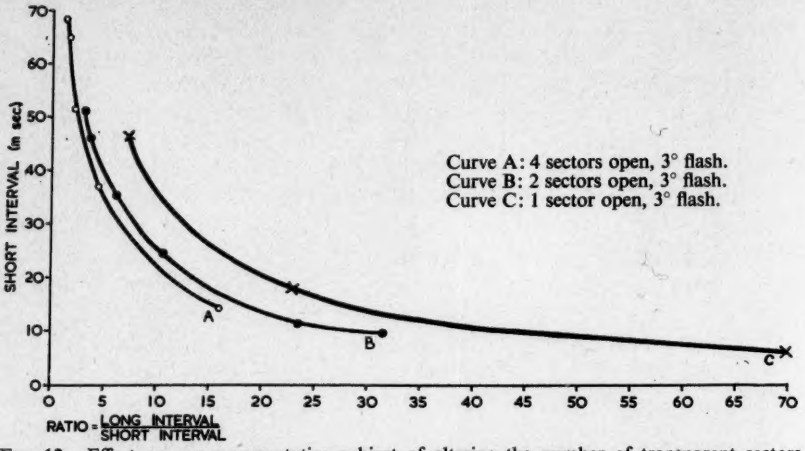

FIG. 12.—Effect on one representative subject of altering the number of transparent sectors. For any given ratio, the fewer the open sectors, the shorter the interval between flashes had to be for stereoscopic fusion.

In both monocular and binocular flicker fusion experiments, it has been similarly established that, the brighter the light, the faster the disk must spin (the shorter the interval between flashes) for flicker fusion to result. But the similarity of this response to changing brightness is superficial. Measurements of comparative brightnesses are only valid at or above the flicker fusion point. It is impossible to compare the brightness of one field at flicker fusion point (one open sector) with the brightness of another field which is still flickering violently (four open sectors)—when stereoscopy can result in either set of conditions.

The temporal summation of stereoscopic fusion might still seem, however, to be merely a function of the persistence of the retinal image—as is said to be the case in flicker fusion. But two findings refute this possibility. The well-marked dissociation between the critical flicker fusion threshold and the stereoscopic threshold indicates not only that the latter function is independent of the former, but that it stems from an entirely different physiological process.

Secondly, the letters emerged from the plane background sequentially:

the first letter to come forward as the end-point approached was the one destined to be the closest. If this were a purely retinal summation of subliminal stimuli, we would expect all the letters to emerge simultaneously, since the retinal sensitivity is not greater for one pair of letters than for another. That the pairs of letters did emerge in sequence indicates a "lag" in integration. Such a "lag" clearly implies a far more complex process than can be explained on the basis of known retinal physiology.

(3) *Effect of Flash Duration.*—Reference to the legend in Fig. 11 indicates that, for the subject J. C., the flash duration was 8·25 msec. when the ratio was 1, and was 15·1 msec. when the ratio was 21. Although the major variable was the change in the ratio L.I./S.I., it was nevertheless observed that at each point in the curve the flash duration had a slightly different value. To be certain of the meaning of the curve the effect of this slight variation in flash duration must first be determined.

Figs 8 and 9 show the mechanism by which flash duration was altered. The alteration of the position of the light beam relative to the disk produced three different changes in the stimulus pattern:

(*i*) It changed the flash duration itself—the primary objective.
(*ii*) It unavoidably altered the ratio of L.I./S.I.
(*iii*) It necessarily changed the brightness of the scene at the stage of flicker fusion.

The importance of the ratio L.I./S.I. has been discussed. It is now useful to separate out the effects of flash duration and brightness, which, in the equipment used, were linked variables.

The brightness of a light the beam of which is interrupted by a sectored disk will depend on the ratio of total transmission time to total non-transmission time. In a disk which has one transparent sector of 360° in width, the brightness will be that of the 36-watt lamp and we can arbitrarily call this one unit of light flux. In another disk with one sector of 3° width, the total light reaching the eye will be 3/360th (or 1/120th) of the full illumination (Fig. 13, Curve A, overleaf).

A disk with one sector of 45° width produced Curve B (Fig. 13) with 45/360th (or 1/8th) of the full illumination. Using a disk with four open sectors of 3° each (Curve C), the total light was 12/360th (or 1/30th) of the total light flux. The increase in brightness produced by a prolonged flash duration could not possibly be the sole explanation for the position of Curve B relative to Curve C. If brightness were the only significant result of increasing flash duration, Curve B should have fallen in the region of the hypothetical Curve D. From the actual position of Curve B, it must be assumed that increasing flash duration had an influence on the duration of the S.I. opposite to that exerted on the S.I. by the factor of brightness *per se*. In Curve A the average flash duration was 3·5 msec., in Curve B it was 7 msec., and in Curve C it was 42 msec. These two factors, brightness

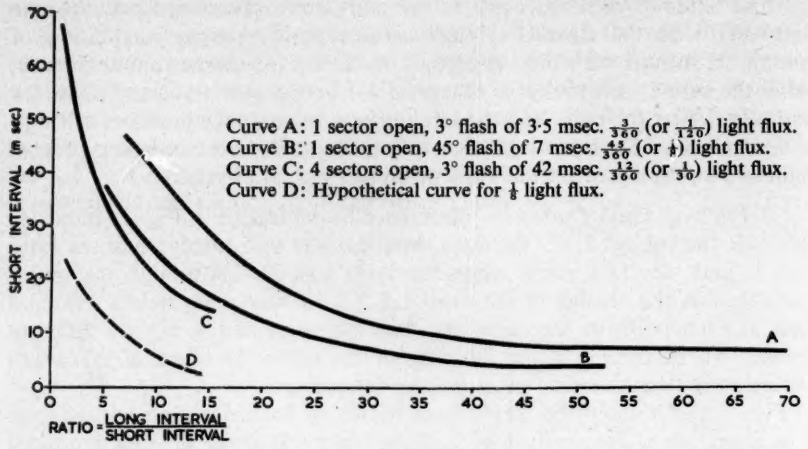
Curve A: 1 sector open, 3° flash of 3·5 msec. 3/360 (or 1/120) light flux.
Curve B: 1 sector open, 45° flash of 7 msec. 45/360 (or 1/8) light flux.
Curve C: 4 sectors open, 3° flash of 42 msec. 12/360 (or 1/30) light flux.
Curve D: Hypothetical curve for 1/8 light flux.
SHORT INTERVAL (m sec.)
RATIO = LONG INTERVAL / SHORT INTERVAL
A
B
C
D

FIG. 13.—Effect of changing flash duration contrasted with effect of changing total brightness. The effect of increasing brightness is distinct from the effect of increasing pulse duration.

of scene and duration of flash, are variables which will cause the basic curve (Fig. 11) to deviate in opposite directions.

The variation in flash duration from one end of the curve (Fig. 11) to the other was from 8·25 to 15·1 msec. (less than 100 per cent. increase). This variation could hardly have affected the position of the curve, since an increase in flash duration of 1200 per cent. (from 3·5 to 42 msec. in Fig. 13) had so small an effect on the S.I. when compared with the large effect due to the change in the ratio S.I./L.I.

Summary

(1) A scene flashed in *one* eye sets up a percept somewhere within the visual system which persists for a measurable period of time (maximum S.I.) and can later be utilized by the brain for a more complex integrative process —stereoscopic fusion. This is memory—specifically memory of the positions of three letters in relation to each other and to the fovea centralis. This is a memory of the *positions* of various objects in the coordinate system of *each* retina. Even a brief recall of the coordinate values of such a monocular stimulation cannot properly be called "parallactic memory", since parallactic information cannot be obtained by one eye. Parallax is determined from the perceptual data of both eyes and these raw data must be "recorded" according to some inherent coordinate system.

(2) If a slightly different coordinate stimulus is presented to the second eye within the necessary time interval (maximum S.I.), the brain will still be able to fuse it with the retinal coordinates of the letters flashed to the first eye, and this will result in a sense of depth.

(3) The period of time after which the first percept has decayed to such an extent that it can no longer be used for fusion was found to range from 6 to 13 msec.—if the visual stimulus were limited to a *single* "couplet" of flashes.

(4) If a *series* of subliminal stimuli are used, this interval is dependent on the time before the next cycle of "couplets" begins. The decay period is related to the interval between the "refresher" stimuli. If the refresher stimulus arrives after a short period and is frequently repeated, the brain can use the first percept for a longer period of time than would otherwise be possible. In physiological terms, the duration of the useful memory of the first percept depends on the temporal summation of stimuli within the system.

(5) This temporal summation is not a retinal function, but is probably an aspect of the central mechanism of binocular stereoscopic fusion. This is in contrast to the phenomenon of flicker fusion, in which the major locus of the summation process resides in the retinal neurones rather than in the brain. Although the phenomenon of retinal persistence must influence all visual perception, there is here a further physiological process, with characteristics of its own which cannot be explained on the basis of known retinal physiology.

(6) The amount of light reaching the eyes and the duration of the exposure are also variables, but of less importance. They have been shown to act in opposite directions.

(7) The shape of the curve of temporal summation is hyperbolic in form and resembles the "learning" curves produced in psychological experiments.

(8) The original purpose of this experiment was to show that stereoscopic vision or binocular fusion results from alternating "attention" by the brain to the retinal images from the two eyes. It was expected by this technique to show that the "Short Interval" would have a fixed value which might represent the time interval (multiple or submultiple) between the recurrent sweeps of a scanning mechanism. It was hypothesised that, if the short interval were made either slightly shorter or slightly longer, it would destroy stereoscopy by an interference phenomenon. This, however, is obviously not the case. Extending the short interval does indeed abolish stereoscopy but shortening it does not alter stereoscopy. In addition, the short interval was found to be a variable factor and not a fixed value in the conditions of repetitive stimulation. It was not possible either to affirm or to deny the existence of a scanning mechanism by this technique.

(9) The experiment has shown that the temporal summation, previously described in "simple" internuncial pools, exists in a similar form for such "higher" or more complex integrative actions of the nervous system as stereoscopic fusion.

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MÖBIUS'S SYNDROME*

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Various terms have been applied to this condition: Möbius's syndrome, congenital facial diplegia, congenital oculo-facial paralysis, nuclear agenesis, and congenital nuclear aplasia. It was originally described by von Graefe (1880), Harlan (1881), and Chisolm (1882). Möbius (1892) collected 43 cases of congenital and acquired cranial nerve palsies and classified them into six groups. One group consisted of six cases of bilateral abducens and facial nerve palsies. Since then Möbius's name has been associated with this condition.

It is relatively uncommon and its bizarre association of lesions may cause affected children to be taken to a paediatrician, an orthopaedic surgeon, an ophthalmologist, or a child psychiatrist. The purposes of the present paper are to record three more cases of this rare condition, to report the absence of any association with Rh incompatibility, and to suggest that the clue to its aetiology may lie in a more detailed investigation of pregnancy histories.

A typical case of Möbius's syndrome shows the following features:

(1) *Bilateral Facial Palsy.*—This is the most obvious feature and it may or may not be complete. If it is not complete the lower part of the face is usually less affected than the upper. This is unlike a supranuclear facial palsy in which the upper part of the face escapes, nor does it resemble a nerve trunk lesion in which the whole side of the face is equally affected.

Another feature characteristic of this condition is the absence of the sagging of the facial tissues, which is so disfiguring a feature of acquired seventh-nerve palsies. If the flesh of the cheek is palpated between finger and thumb it feels peculiarly thin. Contraction of the facial muscles, like that which occurs in cases of Bell's palsy with recovery, is never seen.

Invariably there is a history of sucking and feeding problems in infancy. Dribbling tends to persist into childhood, and when the child is eating, food tends to lodge in the cheeks and has to be pushed out with the fingers.

The orbicularis oculi muscle is defective so that there is incomplete closure of the lids in sleep, infrequent blinking, tearing, and a tendency to a recurrent low-grade kerato-conjunctivitis from exposure.

(2) *Absence of Abduction* of either eye beyond the mid-line, and palsy of the horizontal gaze, so that when looking to either side the child must turn the head.

(3) *Convergence.*—This is usually present but defective. The pupils constrict normally during convergence.

(4) *Vertical Gaze.*—Movements are normal and Bell's phenomenon is intact.

(5) *Convergent Strabismus* is occasionally present.

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(6) *Other Cranial Nerves* may be affected. The hypoglossal nerve may be involved so that the tongue is shrunken and relatively immobile. The motor root of the trigeminal nerve may be affected so that the child has a weak bite. The movements of the soft palate may be defective.

(7) *Other Developmental Anomalies* which occur less commonly are micrognathos, polydactyly, talipes, haemangiomata, and absent pectoralis muscle, and absent breast.

(8) *Mental Deficiency* is often present.

Case Reports

Case 1, a girl aged 4 years, was first seen at the Children's Hospital at the age of 20 weeks. This was the mother's first pregnancy at the age of 27. The father was healthy and there was no consanguinity or history of any familial deformities.

During the first 2 months of the pregnancy the mother had considerable nausea and on one occasion in the second month she fell downstairs. The pregnancy and birth were otherwise normal. The birth weight was 6 pounds 13 ounces. No jaundice or convulsions occurred but from birth there were feeding difficulties. Sucking was performed by compressing the nipple between tongue and palate without any use of the lips.

At the age of 5 months she was seen by Dr. I. H. Beckman of the Children's Hospital who reported:

> The fundi and media are normal. She has a convergent squint which appears to be due to spasm or fibrosis of the internal recti.
>
> At this time one drop of atropine 0·5 per cent. was instilled into each eye and it caused a severe reaction and a temperature of 101° F.

Examination.—At 4 years of age the visual acuity in each eye was 20/30 by the illiterate E test. The pupillary reactions and fundi were normal. An alternating esotropia of 5° was present. Examination of ocular motility revealed normal vertical elevation and depression. Convergence was present but limited. The patient was unable to abduct either eye beyond the mid-line, and when asked to follow a light to one side she sometimes made a great effort and by exercising convergence was able to follow the light a short way with the adducting eye (Fig. 1*a–f*, opposite). Bell's phenomenon was normal.

There was no facial expression at all and although the patient laughed, the sounds of laughter were not accompanied by any change in facial expression. There was some paralysis and atrophy of the left side of the tongue. She was considered to be slightly retarded mentally but she was most co-operative for so young a child.

No haemangiomata were seen. The feet tended to adopt a position of excessive pronation in repose but there was no limitation of dorsiflexion of the foot. The parents said that she was unable to run and that she stumbled readily.

Feeding was still a problem. Food tended to stick in the space between teeth and cheeks and chewing was difficult. The parents said that having a meal was an effort for her. There was some micrognathos.

X-ray Examination.—The skull showed no abnormality.

Electro-encephalogram.—Intrusion of abnormal forms into an otherwise normal record were seen. These patterns were readily suppressed by arousal stimuli and probably arose in subcortical systems.

Blood Group: Mother O;CcDee;
Patient, A;CcDee.

No antibodies other than normal anti-A and B were demonstrable in the mother's serum.

FIG. 1(*a*).—Case 1, looking straight ahead.

FIG. 1(*b*).—Case 1, attempted dextroversion, resulting in *slight convergence.*

FIG. 1(*c*).—Case 1, attempted laevoversion, resulting in slight *convergence. Some pupillary* constriction can be seen.

FIG. 1(*d*).—Case 1, supraversion.

FIG. 1(*e*).—Case 1, infraversion.

FIG. 1(*f*).—Case 1, eyes closed. The closure is incomplete and Bell's phenomenon can be seen to be normal.

Case 2, a boy aged 9, was first seen at the age of 5½ years at the Children's Hospital. The mother also had a normal son, 4 years older than the patient, and she herself was 34 years old when the patient was born. There was no consanguinity nor any family history of facial weakness or abnormal eye conditions. The mother stated that she vomited all through this pregnancy but was well all through the first. The birth was normal. No jaundice or convulsions occurred after birth, but there were considerable feeding difficulties.

Examination.—All facial movements were absent. The tongue was small and shrivelled indicating a bilateral hypoglossal palsy. There was some palatal paralysis and moderate micrognathos. A right talipes equinovarus was present and the patient was severely mentally retarded. He was unable to run and walked with a slow gait in which limb movements seemed restricted in range.

The visual acuity could not be recorded because of the poor mentality. The pupillary reactions to light and the ocular fundi were normal. His eyes were almost fixed in a convergent position at about 25° (Fig. 2, overleaf). Neither eye was able to abduct beyond the mid-line and adduction was limited to a few degrees. The eyes appeared to show no power of convergence. Objects in the right field were watched with the left eye, and the right eye was used for the left field. Moving objects were followed by moving the head. Elevation and depression were normal and Bell's phenomenon was present. The parents stated that he blinked infrequently and that tearing was a constant problem.

X-ray Examination.—The skull was normal.

Electro-encephalogram.—Normal.

Blood Group: Mother, A;CcDee;
Patient, A;CcDee.

No antibodies other than normal anti-B were demonstrable in the mother's serum.

The question of surgical correction of the strabismus was discussed. At first it was considered unnecessary because the child was so mentally retarded, but the parents were anxious to have the boy's eyes straightened because his elder brother was constantly being involved in fights with other children who commented on the younger brother's cross-eyed appearance.

On February 18, 1957, under general anaesthesia the forced duction test in both eyes showed that the movements of elevation, depression, and adduction were free, but that abduction was markedly limited by contracture of the medial rectus. When exposed the lateral rectus looked like a fibrous band. The medial rectus was thickened and contracted and had no elasticity. The insertions appeared to be normal in situation, and no anomalous check ligaments were seen.

A 4-mm. recession of the left medial rectus and a 4-mm. resection of the left lateral rectus were performed. The piece of lateral rectus was sent for microscopy.

Dr. J. Hoogstraten, pathologist to the Children's Hospital, reported that microscopical examination showed "fascicles of dense fibrous tissue resembling tendon or fascia. No muscle fibres were seen. There was no inflammatory infiltrate."

On April 23, 1957, the right eye was operated upon. When the right medial rectus was exposed, it was found to be tightly contracted. No abnormal fascial bands were seen. A 5-mm. recession was performed.

FIG. 2.—Case 2, the patient was too mentally defective to be able to co-operate in any way.

FIG. 3(*a*).—Case 3, looking straight ahead.

FIG. 3(*b*).—Case 3, supraversion. The patient would not co-operate for other photographs.

Case 3, a girl aged 2½ years, was first seen at the age of 4 months. She was the mother's second child but by a different father from the first child. The older child was normal. There was no consanguinity. Attacks of vaginal bleeding lasting about 2 days had occurred every 10 to 14 days during the first 4 months of pregnancy. No other illnesses occurred during the pregnancy.

The birth was normal. Feeding difficulties were experienced from the beginning, but there was no jaundice and no convulsions.

Examination.—The child had bilateral facial palsy, but when she cried or laughed a faint naso-labial fold appeared on the right side. The tongue was small, relatively immobile, and shrivelled on the left side.

No strabismus was present. She was unable to perform ocular conjugate movements to either side or to abduct either eye beyond the mid-line, but vertical elevation and

depression and some power of convergence were present. The pupillary reactions and Bell's phenomenon were normal (Fig. 3*a*, *b*).

She was moderately mentally retarded. She had difficulty in chewing and had a "cross-bite" to the right suggesting some weakness of the motor division of the trigeminal nerve. Micrognathos was marked and she had bilateral talipes equinovarus. Four haemangiomata were present in the following situations: the right side of the neck, the left side of the trunk, the right buttock, and the left big toe.

X-ray Examination.—The skull was normal.

Electro-encephalogram.—Normal.

Blood Group: Mother, A;CcDEe;
Patient, O;CcDe.

No antibodies other than normal anti-B were demonstrable in the mother's serum.

Discussion

The site of the primary lesion and the aetiology of Möbius's syndrome are still not known, although the condition has been recognized for 75 years. Kunn (1895) advanced the view that these lesions were due to failure of the nuclei to develop, *i.e.* nuclear aplasia.

It is obvious that Möbius's syndrome is an intra-uterine developmental defect, but it is not known whether hypoplasia of the muscles of the face and other affected sites is the primary defect so that the poor development of the nerves and cranial nuclei are secondary, or whether the cranial nuclear maldevelopment is the primary lesion and the muscular hypoplasia is secondary (Leszynsky, 1897).

Pathological Findings.—Four pathological studies have been reported (Huebner, 1900; Rainy and Fowler, 1903; Spatz and Ullrich, 1931; Balint, 1936). All four cases showed hypoplasia of the affected cranial nerve nuclei and nerve trunks.

Huebner (1900) reported a finding in his case which may be of significance: that the posterior longitudinal bundle was absent or at least very hypoplastic.

Henderson (1939) considered that the first three cases suggested primary nuclear hypoplasia, whilst Balint's case might have been due to intrapartum haemorrhage. But these studies do not necessarily indicate that cranial nuclear hypoplasia is the primary lesion because failure of development of the muscles would give rise to a secondary degeneration of the cranial nuclei and nerves supplying them.

Relation to Duane's Retraction Syndrome.—Ford (1952) considers that Möbius's syndrome is related to Duane's syndrome and that it is a primary muscle defect. Bedrossian and Lachman (1956) operated upon a patient with this condition and found that the medial and lateral recti were inserted more posteriorly than is normal and that Tenon's capsule was abnormally thickened. They therefore concluded that in their case the primary lesion was a peripheral muscular defect. But the finding of peripheral abnormalities

does not necessarily indicate that the peripheral lesion is the primary defect, for it may be secondary to a primary central defect.

Duane's syndrome is typically unilateral and usually affects the left eye. The patient can rotate both eyes in conjugate gaze to the side opposite to the affected eye, and even in the rare cases of bilateral Duane's syndrome the patient can rotate or adduct each eye towards the opposite side. At operation it has been shown that the condition is due to abnormal tissue bands tethering the eyeball or to fibrosis of the lateral rectus muscle.

Gundersen (1957) has operated on a number of these cases. At operation he found that the lateral rectus appeared to be normal whilst the medial rectus was adherent to the medial wall of the orbit. Histologically, both recti were normal.

Scobee (1952) classified Duane's syndrome into two types:

(1) The lateral rectus is replaced with fibrous tissue.

(2) The medial rectus has abnormal fascial bands which tether the eyeball and prevent abduction.

There is general agreement that Duane's syndrome is due to a primary local anomaly of muscle and fascia. No other muscles supplied by cranial nerves are affected nor are other general developmental anomalies or mental deficiency associated with this condition, as they are with Möbius's syndrome.

In the typical case of Möbius's syndrome, there appears to be a horizontal gaze palsy. Looking to either side is achieved by movements of the head although convergence and elevation and depression are present. Bell's phenomenon is always normal.

It is true that several cases of Möbius's syndrome have been reported in which there has been marked strabismus resembling a strabismus fixus. In our Case 2, there was a marked contracture of each medial rectus muscle, but there were no anomalous fascial bands. Abnormal tethering is the rule in Duane's syndrome, but it does not appear to be so in Möbius's syndrome. Bilateral hypoplasia of numerous muscles supplied by cranial nerves is characteristic of Möbius's syndrome, whilst in Duane's syndrome only one muscle is usually affected.

Breinin (1957a, b) carried out electromyography in two cases of Duane's syndrome, and found almost complete absence of electrical response in the affected lateral rectus in each case. He also carried out electromyography in one case of Möbius's syndrome and was unable to obtain any electrical response from the affected muscles. We consider that these facts support the orthodox view that cranial nuclear agenesis is the essential lesion in Möbius's syndrome.

Relation to Ocular Motor Apraxia.—This interesting condition has only recently been recognized. It has a slight resemblance to Möbius's syndrome in that there is a palsy of voluntary horizontal gaze. Conjugate horizontal movements, however, can be made involuntarily.

Alfano (1955) thought that in this condition the lesion was situated in the middle frontal gyrus. But he argued this on theoretical grounds and, in fact, his case had an occipital encephalocoele which was removed. Reed and Israels (1956) did not accept his localization. They pointed out that the condition resembled the type of horizontal gaze palsy classified as the Oppenheim type by Kestenbaum (1947), who considered that there was no anatomical or pathological basis for deciding the localization of the lesion in this type of palsy.

However, the child reported by Reed and Israels had a normal intelligence quotient and the electro-encephalogram indicated "involvement of subcortical systems associated with the occipital areas". It seems, therefore, that the lesion in ocular motor apraxia is a supranuclear one, probably in the mid-brain in the medial longitudinal bundle (posterior longitudinal fasciculus).

It is perhaps significant that Huebner reported an almost complete absence of the medial longitudinal bundle in his case of Möbius's syndrome.

This structure is unlikely to degenerate to the point of being almost absent as a result of a primary muscle hypoplasia with secondary degeneration of the nerve trunks. This finding of Huebner gives further support to the theory that nuclear agenesis is the essential feature of Möbius's syndrome and to the clinical impression that the defective horizontal movements of these patients are more of the nature of gaze palsies than due to local musculo-fascial anomalies.

In addition to the ocular anomaly the case of ocular motor apraxia reported by Reed and Israels exhibited generalized defects of coordination. We consider that ocular motor apraxia is more closely related to Möbius's syndrome than is Duane's syndrome.

Site of Primary Lesion in Möbius's Syndrome.—The fact that the term nuclear agenesis has been so generally applied to Möbius's syndrome is an indication of the general belief that the muscular manifestations are due to a failure of development of the cranial nuclei.

Duke-Elder (1949) considers that this condition is due to developmental defects of the cranial nuclei and the posterior longitudinal bundle, and we feel there is no reason to question this widely-held opinion.

The cranial nuclei affected in Möbius's syndrome are those of the abducens, facial, motor division of the trigeminal, and the hypoglossal nerves. These nuclei all lie in close proximity in the floor of the fourth ventricle. It is difficult to accept so close an association as being merely fortuitous. It is easy to conceive a noxious influence acting upon the motor nuclei in such a relatively restricted area. But the association with anomalies such as talipes, haemangiomata, and absent breast is more difficult to understand.

Action of Noxious Influences upon the Embryo.—During the last three decades it has been shown repeatedly that the tissues which grow most rapidly in the embryo are those which are most likely to be affected by noxious influences. Stockard (1921) suggested that it was the time of action rather than the type of noxa which decided the nature of the resulting lesions. For three decades this has been the accepted teaching. But recently Duraiswami (1955) injected different substances, such as insulin, cortone acetate, 3-acetylpyridine, and lead nitrate, into developing hens' eggs. He found that although the technique, time of injection, and method of incubation were the same, different malformations were produced. These experiments suggest that, although they may act at the same stage of development, different teratogenic agents may produce different specific anomalies.

It appears that the cranial nuclei which are affected in Möbius's syndrome undergo their most rapid development about the fourth and fifth weeks of intra-uterine life, *i.e.* at the 10-mm. stage (Keibel and Mall, 1912). It seems likely therefore that Möbius's syndrome may be caused by the action of a noxious agent at this period when the mother is barely aware that she is pregnant and hence less likely to remember a minor illness when questioned after the birth of the child.

It is perhaps significant that so few of the reports of Möbius's syndrome in the literature include any mention of a pregnancy history.

Noxa causing Multiple Defects in the Embryo.—It has been shown that irradiation and injection of pitressin or adrenaline to pregnant female mice may cause the development of subcutaneous blebs in the embryos. These blebs result from cerebro-spinal fluid escaping from the fourth ventricle and travelling along planes of least resistance to the subcutaneous tissues of the back and limbs and so causing multiple scattered lesions throughout the body (Bagg and Little, 1924; Bagg, 1929; Ullrich, 1949; Jost, 1953).

The multiple congenital defects which may result from maternal rubella have become well known since they were first recognized by Gregg (1944). It has been shown that measles and possibly influenza in the mother at the appropriate time of pregnancy may produce a rubella-like association of lesions. Reed, Briggs, and Martin (1955) reported a similar case following attempted abortion by taking an excessive quantity of quinine at about the end of the third month of pregnancy.

Ingalls (1956) mentioned three cases in which a mongoloid child followed trauma towards the end of the second month of pregnancy. In one case the mother suffered carbon monoxide poisoning, another was involved in a head-on car accident, and the third had a tooth extraction under gas-oxygen anaesthesia. He pointed out that in mongolism, the nasal bones, the phalanges of the little finger, and the cardiac septum are characteristically stunted, all widely diverse tissues.

Möbius's syndrome may be associated with club feet, haemangiomata,

micrognathos, absent breast, and mental retardation. Other cranial nerves besides the abducens and facial nerves may also be involved. The fact that this condition has so many diverse manifestations is therefore no argument against its being caused by noxa acting upon the embryo.

Other Aetiological Factors.—Heredity appears to play no part in this condition despite a suggestive history in a few cases (Danis, 1945).

Unger, Bork, and Marget (1956) have recently described three cases of congenital abducens palsy which followed neonatal jaundice due to Rh-incompatibility. In our cases, however, there was no history of neonatal jaundice and the blood tests showed that no Rh-incompatibility was present.

Pregnancy History.—It seems probable that if a syndrome of this type is to occur, the noxa must act upon the embryo at about the end of the first month or the beginning of the second month. In our three cases the pregnancy histories seem to be significant. The mother of the first child had a severe fall during the second month. Vomiting occurred throughout the pregnancy in the second case and the mother emphasized that it was unlike her first pregnancy in this respect. In the third case, vaginal bleeding occurred during the first 4 months. These facts may or may not be of significance, but it seems to us that the study of the pregnancy history offers the best hope of discovering the cause of this condition.

Summary

(1) The essential features of Möbius's syndrome are reviewed.

(2) Three cases of the condition are reported.

(3) The essential nature of the lesions are discussed. It is concluded that cranial nuclear agenesis is the most acceptable concept.

(4) The aetiology of the condition is discussed.

(5) It is suggested that more careful pregnancy history-taking may shed light on this problem.

Dr. Bruce Chown of the Rh Laboratory of Winnipeg kindly supplied the information concerning the blood groups of patients and mothers. The electro-encephalographic reports were obtained through the courtesy of Dr. M. G. Saunders of the E.E.G. Department of the Winnipeg General Hospital.

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Clostridium sporogenes	S	R
Corynebacterium diphtheriae	S	S
Corynebacterium diphtheroides	S	S
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Brit. J. Ophthal. (1957) 41, 741.

ROLE OF FAT EMBOLI IN DIABETIC RETINOPATHY*

BY

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THE association between diabetes mellitus and disturbance of fat metabolism has long been recognized, and the lipoidal nature of the diabetic vascular changes has been emphasized by many workers particularly with reference to the retinal and renal changes. It is only in recent years, however, that fat emboli have been reported in association with diabetic vascular disease. *Thus Wilens, Elster, and Baker (1951)* demonstrated that the deposition of fat in the lesions of diabetic glomerulosclerosis is directly proportional to the severity of the renal involvement. *Hartroft (1955) found that fat emboli* in choline-deficient rats eventually gave rise to glomerular lesions resembling human diabetic glomerulosclerosis, and Kent (1955) showed that fat emboli indistinguishable from the traumatic variety were to be found much more frequently in diabetics than in non-diabetics.

Retinal vascular lesions following traumatic fat embolism were reported by Czerny (1875), but the possibility that a similar process might play a part in the pathogenesis of diabetic retinopathy has attracted little attention, although it is noteworthy that Morgan (1949) reported that a case of traumatic fat embolism showed a fundus picture not unlike that occasionally seen in the diabetic, and that Urbanek (1933) remarked upon the similarity of the ophthalmoscopic picture seen after fat embolism to that in senile diabetics with arteriosclerosis.

In view of these facts, the present investigation was undertaken to examine microscopically the retinal and renal lesions produced by experimental fat emboli in an attempt to evaluate their possible role in the pathogenesis of diabetic vascular disease.

Material and Methods

A total of eighteen cats received bi-weekly intravenous injections of fat (1 ml./kg. bodyweight) over a period varying from one week to 2 months. The time interval elapsing between the last injection and the immediate *post-mortem* examination of the retina and kidney also varied from 2 hours to 6 months. Although four varieties of fat were used in different animals (olive oil, arachis oil, and animal fat derived from both the cat and rabbit), no histological differences were noted in either the retinal or renal lesions produced by them.

* Received for publication July 16, 1957.

Findings

Retinae examined within 6 hours of a single intravenous injection of fat show that practically the entire retinal arteriolar and capillary bed is filled with a mass of fat disposed in the form of long columns in some vessels and globules of varying size in others. In the latter cases, sharply circumscribed extra-vascular aggregations of fat may be seen in the immediately adjacent retinal stroma (*Fig. 1*).

FIG. 1.—Aggregations of fat within the distended arteriolar lumen with localized fatty infiltration into the adjacent retinal tissues. × 166.

In the retinae of animals which had received eight injections of fat, a marked feature was the impaction of isolated fatty globules within the capillary lumen to form multiple localized capillary dilatations, which in many cases were surrounded by a perivascular mantle of fat (Figs 2 and 3, opposite). Although these superficially resembled capillary micro-aneurysms, it must be emphasized that in none of these lesions was any histological evidence of change in the vessel wall found.

Retinae examined after twelve fat injections show that both the intra- and extravascular fatty deposits tend to become progressively more numerous. There were in addition scattered localized areas of retina showing complete capillary collapse, in some of which small partially absorbed haemorrhages were visible. The most noteworthy feature at this stage, however, was the presence of multiple minute fatty globules in both the perivascular spaces of the larger arterioles and also within the arteriolar walls themselves.

A finding of considerable interest was noted in the retinae examined 6 months after the last fat injection. Even after this period scattered intracapillary and extracapillary deposits of fat were still visible, the former in

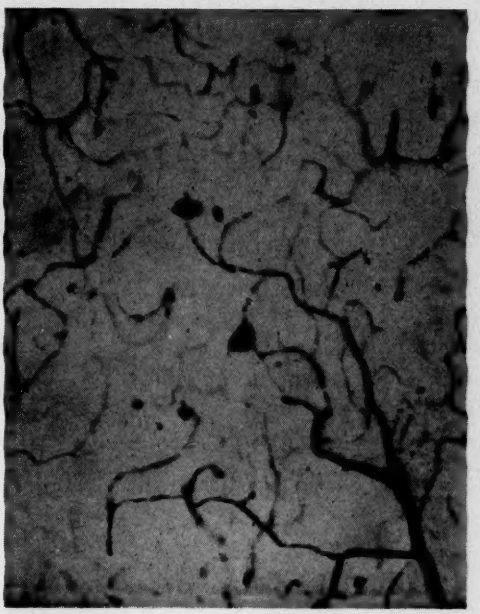

FIG. 2.—Retinal capillaries injected with Indian ink. Isolated fat globules are visible both within the capillary lumen and in the perivascular spaces. × 93.

FIG. 3.—Retinal capillaries injected with Indian ink. Isolated fat globules are visible both within the capillary lumen and in the perivascular spaces. × 187·5.

some cases associated with a marked localized capillary dilatation. The deposits along the arterioles however, had completely disappeared and

although the fatty deposits were in some areas associated with a localized zone of capillary collapse, no evidence of degenerative change in any of the capillary walls was apparent.

The renal embolic lesions produced in this investigation consisted essentially of multiple sharply-circumscribed globules of fat impacted within the glomerular capillaries (Fig. 4). The histological appearances of these glomerular lesions were quite unlike those of diabetic glomerulosclerosis, for not only were the glomerular capillary walls intact but there was also a complete absence of the glomerular nodules pathognomonic of the human renal lesion.

FIG. 4.—Renal glomerulus showing multiple fat globules. × 510.

Discussion

Whilst circumstantial evidence can be adduced directly associating the retinal and renal lesions of diabetes with a disturbance of fat metabolism, the findings of this investigation do not support the hypothesis that such

lesions can be produced by fat embolism alone. Although the experimentally induced retinal lesions may superficially resemble the diabetic micro-aneurysm, the lack of degenerative and infiltrative changes of the capillary wall must sharply differentiate such inert capillary dilatations from those associated with diabetic vascular disease. These results, however, do not preclude the possibility that the lipoid constituents of the retinal and renal lesions may be directly due to a deposition of plasma fat in a different physico-chemical form than that used in these experiments. Indeed, such a mechanism is possibly suggested by the work of Keiding, Mann, Root, Lawry, and Marble (1952), who found a superficial relationship between the presence of diabetic retinopathy lesions and the elevation in the plasma of macromolecular lipoproteins of the Sf 12–20 class as identified by the ultracentrifuge.

It must be emphasized, however, that such a postulate as yet entirely lacks either clinical or experimental confirmation, but further investigation into this aspect of the problem might well result in a most valuable addition to our as yet fragmentary knowledge of the complex factors involved.

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Brit. J. Ophthal. (1957) **41**, 746.

COMBINED ACTION OF DIAMOX AND POTASSIUM BICARBONATE IN THE TREATMENT OF CHRONIC GLAUCOMA*

BY

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IT has been well established that Diamox causes excretion of cations, especially sodium and potassium, and that in conditions of sodium depletion potassium may be excreted in place of sodium (Milne, 1956). In fact the administration of potassium bicarbonate will increase the systemic effects of Diamox.

We have already drawn attention to the correlation between cation excretion and fall in intra-ocular pressure after Diamox (Campbell, Jones, and Tonks, 1956), and were therefore interested to discover whether potassium bicarbonate would have a potentiating effect on the action of Diamox in cases of chronic glaucoma.

In common with other observers (Becker and Middleton, 1955; Kupfer, Lawrence, and Linnér, 1955), we have noticed that patients under treatment with Diamox often complain of paraesthesia and that this symptom is sometimes associated with a relatively low level of blood potassium. It is interesting to note in this respect that Becker and Middleton have reported the relief of paraesthesia and other side-effects by the addition of potassium chloride given by mouth.

On a pharmacological basis, the continued use of Diamox could not be expected to be beneficial in the treatment of chronic glaucoma, since a single dose engenders a state of acidosis from which the body may take 2 to 3 days to recover (Maren and Wadsworth, 1955; Hanley and Platts, 1956). In fact, Arruga (1955) pointed out that, whenever Diamox has been used over long periods with success, it has always been employed in combination with miotics. It is highly probable that the latter masked the diminishing effect of Diamox. Our experiments were designed to elucidate this point as well as to investigate the effects of the addition of a potassium salt.

Experiments

We made a detailed study of the effect of Diamox in three patients affected with open angle glaucoma. They were selected from the glaucoma clinic

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because they were unwilling to undergo any further surgical treatment, and their glaucoma had ceased to be controlled adequately either by miotics alone, or by the administration of Diamox in frequent doses (usually 250 mg. once or twice daily). In each patient renal function was normal.

On admission the patients were given a uniform diet as described previously (Campbell, Tonks, and Jones, 1956). The food and water intake was recorded, the sodium intake being not more than 44 mEq. in 24 hours, and the water intake being controlled so as to maintain a regular state of hydration.

The following investigations were made in sequence:

(*a*) Diurnal variation of the intra-ocular pressure, in the resting state (mm. Hg Schiötz).
(*b*) A study of the effect upon intra-ocular pressure of a daily single dose of 250 mg. Diamox on consecutive days.
(*c*) A study of the combined effect of Diamox (250 mg. daily) and potassium bicarbonate (1 g. three times a day) administered at 7 a.m., 2 p.m., and 7 p.m.
(*d*) The correlation of the effects of Diamox on intra-ocular pressure with systemic effects, in respect of the variations in urinary volume, and sodium and potassium excretion.

Case Histories

Case 1 (Unoperated Bilateral Glaucoma) in a woman aged 72 who was under continuous observation for a period of 20 months before admission.

When first seen (5.5.54) she complained of poor visual acuity in the right eye.

Right Eye.—Visual acuity counting fingers, not improved by glasses. Cupped disc. Ocular tension 56 mm. Hg. Virtually no residual field.

Left Eye.—Visual acuity 6/18, with glasses 6/9. Normal ocular tension. Full field.

Intra-ocular pressure in the right eye responded to 1 per cent. eserine drops, and one week later the ocular tension was 28 mm. Hg in the right eye and 32 mm. Hg in the left eye. The drops were then prescribed for both eyes. Intra-ocular pressure remained unchanged for 3 months, when eserine irritation developed, and the drops were changed to 2 per cent. pilocarpine. The intra-ocular pressure appeared to be controlled satisfactorily until November, 1955, when it rose to 40 mm. Hg in the right eye. It was again controlled by the addition of 0·5 per cent. eserine to the 2 per cent. pilocarpine drops.

The patient was transferred to the Glaucoma Clinic in January, 1956, when her afternoon records of intra-ocular pressure were found to be unexpectedly high, *viz.* right eye 40, left eye 35 mm. Hg. She was given Diamox 250 mg. daily and eserine 0·5 per cent. in the right eye, and pilocarpine 2 per cent. in the left eye three times a day. The intra-ocular pressure was reduced after one week to 28 mm. Hg and at the end of a month to 24 mm. Hg in each eye. Diamox was then reduced to 250 mg. every other day, and the intra-ocular pressure was controlled for a period of 3 months.

On May 9, 1956, she complained of severe tingling 4 hours after taking Diamox and was found to have a rather low blood potassium (4·1 mEq. per cent. compared with the normal range of 4·4 to 5·6 mEq. per cent). The intra-ocular pressure was taken in the

afternoon and found to be 30 mm. Hg in each eye, and she was therefore admitted for fuller investigation. At this time the visual acuity in the right eye was perception of light; in the left eye it was 6/9 with slight contraction of field. Both eyes still showed an open angle on gonioscopy.

(*a*) *Diurnal Variation.*—Records of intra-ocular pressure were taken for a period of 4 days with the patient at rest in bed and receiving no treatment. Fig. 1(*a*) shows that there were wide excursions in the intra-ocular pressure which tended to lessen with rest.

(*b*) *Effect of Diamox Alone.*—There was a tendency for the intra-ocular pressure to rise in the late afternoon, so that Diamox (250 mg.) was given at 4 p.m.

On the first day there was a good response, but on the second day the response was almost negligible (Fig. 1*b*), *i.e.* the patient very quickly became resistant. After an interval of 3 days Diamox again produced a response, but the intra-ocular pressure rose again above the initial level in less than 24 hours.

(*c*) *Effect of Diamox plus Potassium Bicarbonate.*—The addition of potassium bicarbonate 1 g. three times daily produced a well-sustained response to a daily dose of Diamox (Fig. 1*c*). The patient was discharged on this treatment without miotics.

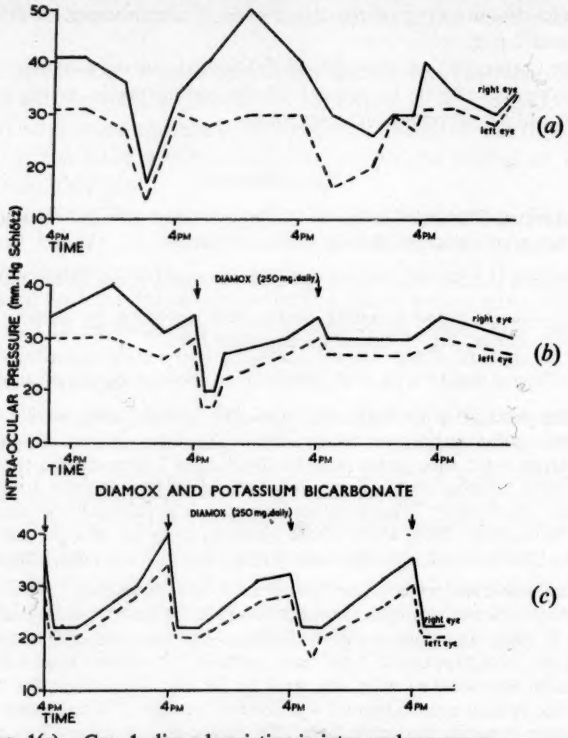

FIG. 1(*a*).—Case 1, diurnal variation in intra-ocular pressure.

FIG. 1(*b*).—Case 1, diminishing effects of Diamox.

FIG. 1(*c*).—Case 1, adjuvant effect of potassium bicarbonate 1 g. three times a day.

Subsequent Progress.—Later tests were conducted as an out-patient, intra-ocular pressure being recorded before, and 1 hour after, a dose of Diamox, given on each occasion at the appropriate time (Table).

TABLE
PROGRESS OF CASE 1 ON DIAMOX AND POTASSIUM BICARBONATE

Date	Time of Dose (p.m.)	Intra-Ocular Pressure (mm. Hg)			
		Before Diamox		1 hr after Diamox (250 mg.)	
		Right	Left	Right	Left
7.6.56	4.0 5.0	41	31	35	27
22.6.56	2.30 3.30	35	31	27	23
5.8.56	3.0 4.0	25	28	20	23
10.8.56	3.0 4.0	26	23	23	20
24.8.56*	3.0	26	23		
7.9.56	3.30	24	27		
15.10.56	3.45	27	23		
7.12.56	3.0	25	22		
15.2.57	3.30	23	20		

* Further tests with Diamox were unnecessary from this date.

On a combined therapy of Diamox and potassium bicarbonate, progress has been quite satisfactory for 8 months. The visual acuity in the left eye is still 6/9, with no further loss in the visual field, and the blood potassium and sodium have remained within normal limits.

Case 2 (Bilateral Glaucoma with Iridencleisis in the Left Eye) in a woman aged 64 who first attended hospital on September 9, 1955, complaining of deterioration of vision in the left eye.

Right Eye.—Visual acuity 6/24. Intra-ocular pressure 25 mm. Hg. Visual field reduced to half; mainly temporal loss. Early cupping of the disc.

Left Eye.—Visual acuity 6/36. Intra-ocular pressure 56 mm. Hg. Total loss of nasal visual field with reduction of temporal field. Marked cupping. Steamy cornea.

Gonioscopy showed an open angle in both eyes.

She was admitted on the same day for intensive treatment of left eye with eserine. The intra-ocular pressure fell to 40 mm. Hg, and with one dose of 250 mg. Diamox to 30, but rose again to 60 mm. Hg. Left iridencleisis was therefore performed on the third day. The intra-ocular pressure remained high for 9 days, and was reduced by a daily dose of Diamox 250 mg. On discharge on the 19th day intra-ocular pressure was 35 mm. Hg

and it finally fell to 28 on continuation of the same treatment by the 21st day. Diamox was discontinued and 1 per cent. pilocarpine drops substituted, but the intra-ocular pressure rose again to 56 mm. Hg after 2 weeks and could not be controlled by increasing the strength of pilocarpine to 2 per cent.

On November 1, 1955, Diamox 250 mg. twice a day and pilocarpine 2 per cent. were resumed. The intra-ocular pressure remained normal (25) for over 3 months. Diamox was then discontinued and the pilocarpine reduced to 1 per cent., but on April 6, 1950, the intra-ocular pressure again rose to 45 mm. Hg. Diamox 250 mg. every other day was again effective and further operation was not considered.

The intra-ocular pressure in the right eye had so far given no cause for concern, but on April 20, 1956, it rose to 32 mm. Hg. It so happened that the patient was now attending in the afternoon whereas the previous records had been made at a morning clinic. She was therefore admitted on April 23, 1956, to the Research Department for observation.

(*a*) *Diurnal Variation.*—With rest in bed and no treatment, the intra-ocular pressure did not rise above 34 mm. Hg in the left eye and 28 mm. Hg in the right eye for 2 days, but was highest each day in the late afternoon. On the morning of the third day the left eye developed acute glaucoma. A dose of Diamox produced an immediate fall in intra-ocular pressure, but in the afternoon eserine 0·5 per cent. had to be used in the left eye, and two more doses of Diamox were given, one at 4.30 p.m. which was immediately vomited, and a second at 8 p.m. with good effect.

(*b*) *Effect of Repeated Daily Doses of Diamox* (Fig. 2*a*, opposite).—After an interval of 4 days, when the patient remained at rest, dosage with Diamox was resumed. It was administered at 4 p.m. each day, *i.e.* at the time when the intra-ocular pressure began to rise. The diminishing effect of daily repetition of the drug is particularly well seen in the case of the right eye. The intra-ocular pressure in the left eye was barely affected and had to be controlled by the additional use of eserine drops at 10 p.m.

Once again, after 2 days without Diamox, the left eye developed acute glaucoma. The intra-ocular pressure rose again to 61 mm. Hg and had to be reduced with intensive eserine. The intra-ocular pressure in the right eye rose at the same time to 40 mm. Hg. It was therefore decided to explore the effect of potassium bicarbonate as an adjuvant.

(*c*) *Effect of Diamox plus Potassium Bicarbonate* (Fig. 2*b*, opposite).—In the 4 successive days immediately following the acute rise in tension, the patient was given a daily dose of 250 mg. Diamox at 4 p.m. together with 1 g. potassium bicarbonate at 7 a.m., 2 p.m., and 7 p.m. There was a striking improvement in the response to Diamox and a steady decline in the maximum intra-ocular pressure in both eyes.

The patient was discharged on this treatment, and on two occasions in the glaucoma clinic (after intervals of one week and of 3 weeks) the intra-ocular pressure fell to 17 and 20 mm. Hg in the right and left eyes respectively, 2½ hours after a test dose of Diamox.

A further check as an in-patient 2 months later showed that the control of intra-ocular pressure was well maintained even without miotics. In this test potassium biphosphate in doses of 2 g. three times a day was substituted for potassium bicarbonate. Its effect was slightly less marked than that of potassium bicarbonate.

The patient has continued under treatment with Diamox and potassium bicarbonate for a total period of 8 months. Her blood potassium has remained within normal limits, and except for one occasion the intra-ocular pressure in the left eye has not risen above 25 mm. Hg, and that of the right eye above 20 mm. Hg. The visual acuity (with correction) is 6/18 in the right eye and 6/60 in the left eye. The visual field in the right eye shows no further loss.

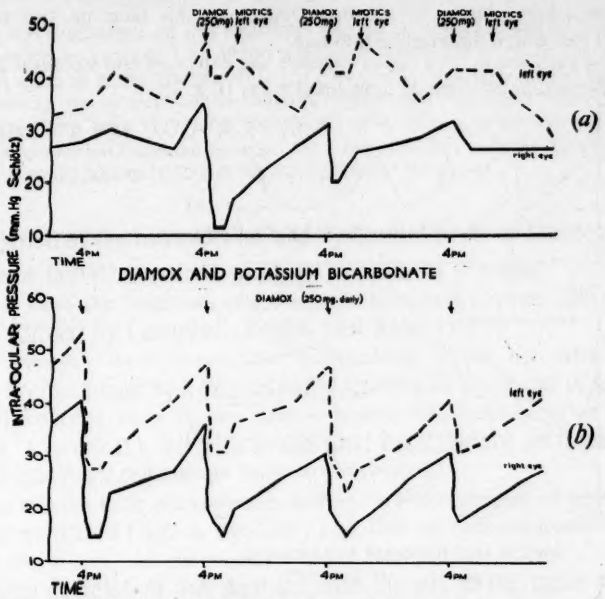

FIG. 2(*a*).—Case 2, diminishing effects of Diamox.

FIG. 2(*b*).—Case 2, adjuvant effect of potassium bicarbonate, 1 g. three times a day.

Case 3 (Bilateral Glaucoma—with Non-filtering Iridencleisis in the Right Eye, and Iridencleisis plus Cyclodialysis giving Active Filtration in the Left Eye) in a man aged 45 who had been under continuous observation for 8 years before coming to the glaucoma clinic.

His initial state in 1948 was visual acuity 6/9 and intra-ocular pressure 40 mm. Hg in the right eye, and visual acuity 6/18 and intra-ocular pressure 35 mm. Hg in the left eye.

On gonioscopy both eyes had an open angle. Both visual fields were full, and the optic discs showed early glaucomatous cupping.

He was treated with miotics for several months until early in 1949 when the intra-ocular pressure rose again to 40 mm. Hg in each eye. Bilateral iridencleisis was performed but miotics were necessary post-operatively.

In November, 1954, the left eye developed acute glaucoma, the intra-ocular pressure being 48 mm. Hg, and a cyclodialysis was performed followed by a paracentesis 6 weeks later. After this, filtration was maintained in the left eye, but the right still required treatment with miotics. There was only a slight loss in the nasal fields after 7 years' treatment, but the visual acuity had diminished to 6/18 in the right eye and 6/36 in the left.

In January, 1956, the intra-ocular pressure rose to 45 mm. Hg in the right eye and 32 mm. Hg in the left. On this occasion it responded immediately to Diamox. A maintenance dose of 250 mg. every other day was continued for 4 months, miotics being still necessary in the right eye. The visual acuity was adversely affected by the miotics, and in May, 1956, the patient complained that his vision became misty every afternoon. At this point he was admitted to the Research Department for fuller investigation.

Diurnal Variation and Response to Diamox

(*a*) In the resting state the intra-ocular pressure was observed to rise each day soon after 11 a.m. (Fig. 3*a*, overleaf).

(*b*) The administration of 250 mg. Diamox at this hour on two successive days (Fig. 3*b*) met with a diminishing response.

(*c*) The daily fall in intra-ocular pressure was enhanced and sustained by the addition of 1 g. potassium bicarbonate three times a day (Fig. 3*c*).

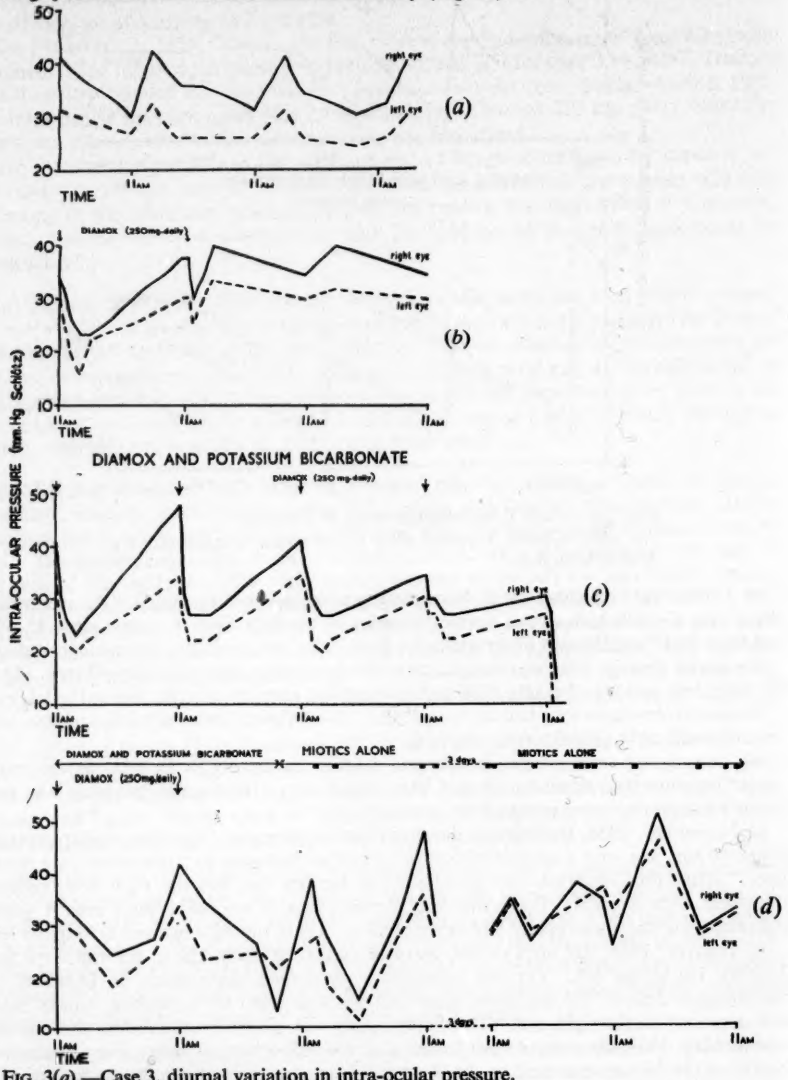

FIG. 3(*a*).—Case 3, diurnal variation in intra-ocular pressure.

FIG. 3(*b*).—Case 3, diminishing effect of Diamox.

FIG. 3(*c*).—Case 3, effect of Diamox and potassium bicarbonate 1 g. three times a day.

FIG. 3(*d*).—Case 3, repeated test showing rise in intra-ocular pressure after withdrawal of Diamox and potassium bicarbonate even with use of miotics.

The patient was discharged on this treatment and his condition remained satisfactory for 3 months, when on October 1 his blood potassium was found to be 22 mg. per cent. On testing him again as an in-patient, we found that on the first day Diamox alone promoted a reasonable fall in intra-ocular pressure, while with potassium bicarbonate on subsequent days there were very large excursions (Fig. 3*d*). On withdrawal of both drugs the diurnal variation increased in extent for a few days, but with the succeeding rise in tension it was again necessary to use miotics to control the peaks.

Correlation of the Intra-Ocular and Systemic Effects of Diamox

For the sake of brevity the three cases are considered together:

(*a*) In each case the systemic reaction to Diamox followed the pattern previously described by Campbell, Tonks, and Jones (1956).

(*b*) With repeated daily doses the diminishing effect on intra-ocular pressure was accompanied by a diminishing excretion of urine and of sodium. This was evident not only in the first 6 hours immediately after taking Diamox (Fig. 4, overleaf), but also in the total excretion for 24 hours. As sodium was conserved, potassium excretion increased.

(*c*) In cases treated with potassium bicarbonate the excretion of potassium was of course increased (Fig. 5, overleaf) and that of sodium markedly decreased. Diuresis was well sustained.

(*d*) A striking correlation was seen between the pH of the urine and the intra-ocular pressure (Figs 6 and 7, overleaf). A fall in the latter coincided with a marked increase in alkalinity of the urine.

Results

It is evident that solitary records of intra-ocular pressure taken in the out-patient department are not a true indication of the progress of the disease, unless they are recorded at the time when the "peak" of intra-ocular pressure normally occurs. This varies in individual cases and can only be discovered by recording the diurnal variation for several days in the resting state as an in-patient. Diamox can then be administered subsequently at the optimum time, *i.e.* when the intra-ocular pressure is beginning to rise.

It is advisable to discover the degree of response to a particular dose of Diamox. Each of our three cases, on empirical treatment with Diamox before admission, had shown a decline in response to treatment, and this was confirmed by the test. There was a diminishing fall in intra-ocular pressure on successive days when Diamox was administered. This phenomenon was associated with a decline in the systemic effect, as shown by a decrease in diuresis, decreased excretion of sodium, and a return to acidity of the urine. The significance of the correlation of these changes is discussed later.

The addition of potassium bicarbonate in doses of 1 g. three times daily proved surprisingly successful in combination with one daily dose of 250 mg Diamox. Not only were the "side-effects" prevented, but the intra-ocular

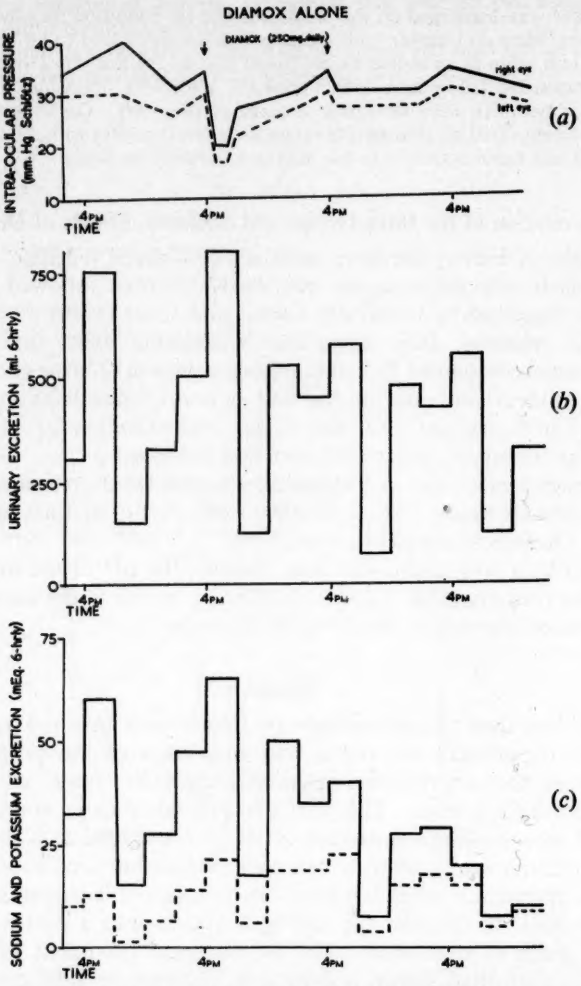

FIG. 4.—Case 1, diminishing effect of Diamox on: (*a*) intra-ocular pressure, (*b*) urinary excretion, (*c*) sodium and potassium excretion.

pressure was controlled. The patients were discharged on this treatment and when they were re-tested in hospital after an interval of 2 to 3 months the response was found to be maintained. Two of them (Cases 1 and 2) had shown no abnormal rise in intra-ocular pressure and no side-effects over a total period of 3 months. In the third case the dose of potassium bicarbonate had to be decreased, as he was found to have a rather high level of blood potassium after 2 months.

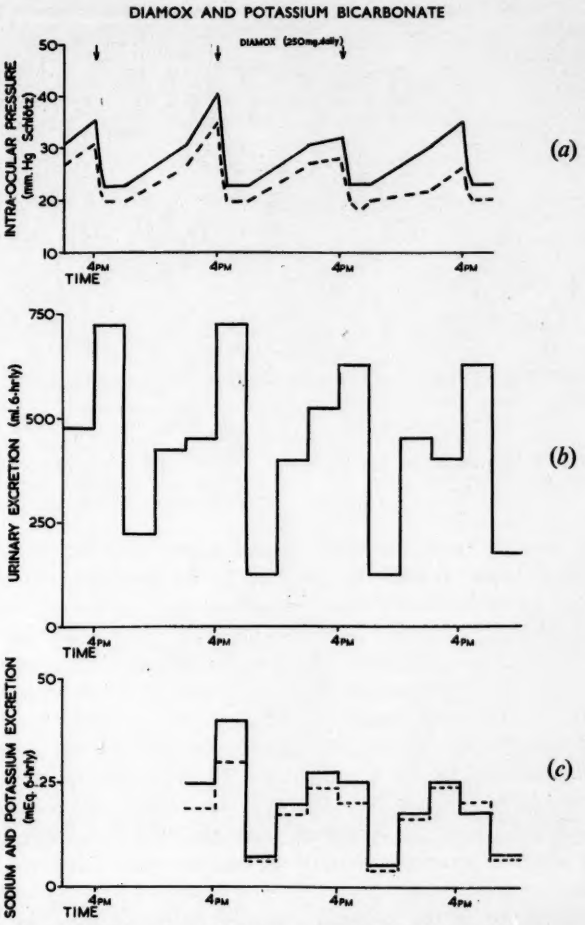

FIG. 5.—Case 1, effect of Diamox and potassium bicarbonate 1 g. three times a day on: (*a*) intra-ocular pressure, (*b*) urinary excretion, (*c*) sodium and potassium excretion.

In the follow-up of cases, the intra-ocular pressure was also checked in the out-patient department as described in Case 1, and blood potassium estimates were carried out at intervals of a few weeks.

Therapy with Diamox must be confined to individuals in whom there is no abnormality of renal function.

Discussion

The problem of resistance to Diamox is an interesting one, and as Breinin and Görtz (1954) have pointed out, it is "one of the most characteristic

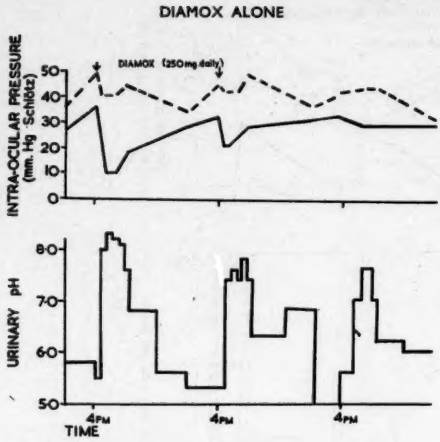

FIG. 6.—Effect of Diamox alone on: (*a*) intra-ocular pressure, (*b*) urinary pH.

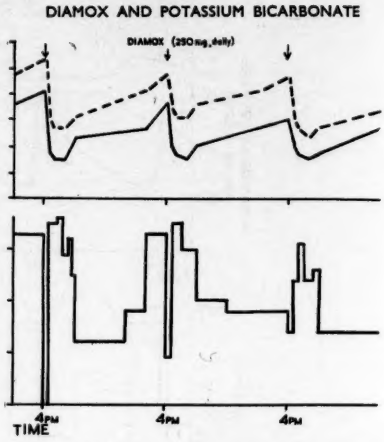

FIG. 7.—Effect of Diamox and potassium bicarbonate (1 g. three times a day) on: (*a*) intra-ocular pressure, (*b*) urinary pH.

findings in acetazolamide medication and constitutes the central problem towards which research must be directed". In the light of this statement the assertion made by Becker and Middleton (1955) that "it now appears firmly established that selected patients with otherwise uncontrolled glaucoma can be maintained (on Diamox) without loss of vision or field and without significant systemic or ocular toxicity" is a misleading one, particularly as the majority of their cases received miotics as well as Diamox.

In other spheres Diamox has been employed as a diuretic, *e.g.* in cases of cardiac oedema, and there is abundant evidence that its action is self-limiting (Counihan, Evans, and Milne, 1954). The increase in urinary volume, increase in urinary pH, and increased excretion of bicarbonate, sodium, and potassium which it promotes initially all decline when it is given in repeated daily doses.

The relationship of the systemic changes to the changes in intra-ocular pressure is not yet fully known, but there is a parallel response in both after a single dose of Diamox (Campbell, Tonks, and Jones, 1956), and this response diminishes in both after repeated daily doses as shown by our present results. These phenomena occur in both unoperated and operated eyes.

The self-inhibiting effect of Diamox is said to be entirely due to a reduction of the filtered glomerular load of bicarbonate secondary to the systemic acidosis produced (Counihan, Evans, and Milne, 1954), and excretion of bicarbonate is said to fail when the bicarbonate plasma level falls below 16 mEq/l. Maren (1955), on the other hand, states that it is the total quantity of base lost or net body acidosis which inhibits the renal effect.

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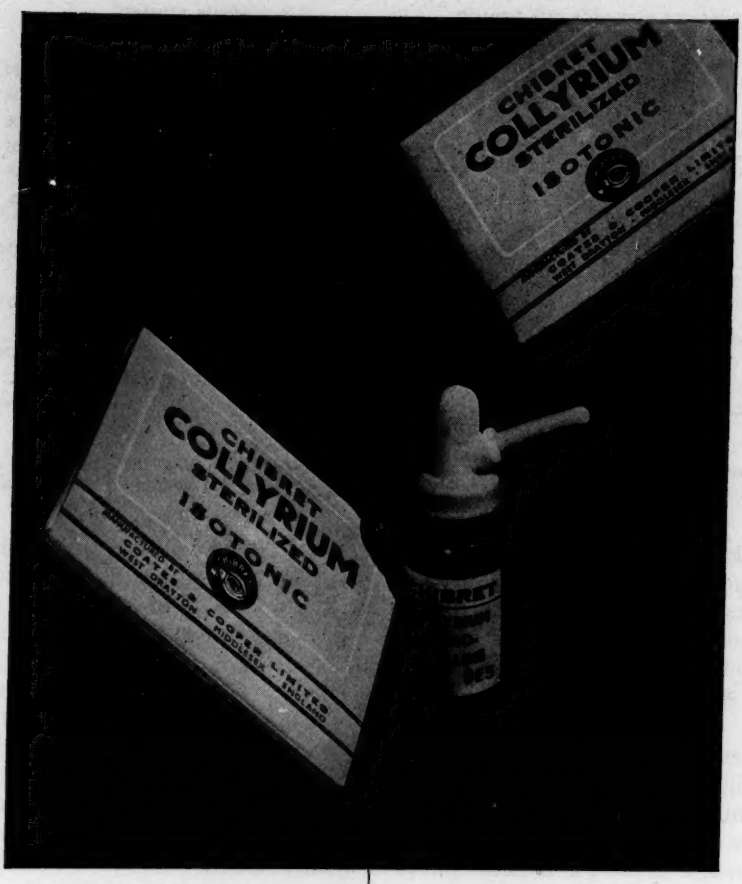

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Hanley (1956) has shown that continued administration of Diamox after resistance has set in will maintain the depression of plasma bicarbonate and the systemic acidosis, but will not cause any further excretion of bicarbonate.

The adjuvant effect of an increased potassium bicarbonate intake may therefore be due either to the addition of "base" or to added bicarbonate ion. Our test in Case 2, when potassium biphosphate was used in place of potassium bicarbonate, suggests that it may be due to added "base".

The kidney has the ability to conserve sodium or potassium as required; *e.g.* in dietary sodium depletion it favours excretion of potassium bicarbonate (Counihan and others, 1954), and in potassium deficiency it favours sodium excretion (Evans, Hughes-Jones, Milne, and Steiner, 1954). Our patients were maintained on a comparatively low sodium intake and the administration of potassium bicarbonate therefore favoured the conservation of sodium.* It is interesting to compare this with the finding of Kinsey, Camacho, Cavanaugh, Constant, and McGinty (1955) that rabbits, which were resistant to the action of Diamox and showed no fall in intra-ocular pressure, were made responsive by giving them an increased amount of salt in their diet.

Obviously the problem of the distribution of electrolytes in relation to the maintenance of intra-ocular pressure is a fascinating one. The distribution of the ionic constituents of the aqueous humor after Diamox (Langham and Lee, 1955, 1957; Falbriard, Sanz, Zender, and Franceschetti, 1955) suggests that its effect on the intra-ocular pressure is not the direct outcome of the inhibitory effect of the drug on carbonic anhydrase but is probably due to an alteration in the osmotic balance between the blood and aqueous humour, independent of its renal action. Duke-Elder, Perkins, and Langham (1956) have suggested that the effect of Diamox on intra-ocular pressure arises from a decrease in the base-binding capacity of the blood below normal, which in turn results in a lowered rate of formation of intra-ocular fluid.

Summary

(1) The effects of a daily dose of 250 mg. Diamox have been examined in relation to the problem of "resistance" to the action of the drug.

(2) A diminishing fall in intra-ocular pressure on successive days corresponded with a decline in the systemic effects of the drug as shown by the changes in the pattern of urinary excretion.

(3) The administration of potassium bicarbonate in doses of 1 g. three times a day, together with 250 mg. Diamox daily, restored the response and proved effective in controlling the intra-ocular pressure for a considerable period. It also prevented the occurrence of unpleasant side-effects.

(4) This treatment has certain advantages over the use of Diamox combined with miotics, but before it is adopted it is recommended that

* A similar state of affairs continues under Diamox therapy (Milne, 1956).

investigations should be carried out with the patient in hospital in respect of urinary function, diurnal variation of intra-ocular pressure, and the response of the individual to Diamox and potassium bicarbonate.

(5) During treatment the intra-ocular pressure and the blood potassium should be estimated at regular intervals.

(6) The mechanism of the combined action of Diamox and of potassium bicarbonate on intra-ocular pressure is discussed in relation to its systemic effects.

Our thanks are due to Mr. Archer-Hall and Mr. Charles Rudd, for permission to investigate their cases, and to Mrs. Eva Nelson for technical assistance.

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Brit. J. Ophthal. (1957) **41**, 759

CASE NOTES

THREE UNUSUAL CORNEAL GRAFTS*

BY

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At a recent hospital demonstration of corneal graft cases three examples, which are described below, evoked special interest.

Case 1, Contralateral Corneal Autoplasty.—There are two types of case in which the patient supplies his own donor corneal graft, *i.e.* an autograft. One type may be termed ipsilateral autoplasty when the graft is provided by the cornea which itself is to be grafted, and the other, contralateral autoplasty, when the graft comes from the other cornea of the same patient.

Ipsilateral autoplasty is performed when a disc of cornea having a clear area is fashioned so that it can be rotated to replace an opaque area over the pupil (Kraupa, 1914). Another method is to exchange a disc of scar tissue over the pupil with a clear graft from the periphery of the same cornea (Morax, 1913).

Contralateral autoplasty is performed when the graft is obtained from the cornea of the patient's other eye. Plange (1908) has reported such an example, using a lamellar graft.

Whilst it is often vouchsafed to plastic surgeons to use skin autografts in their treatment of burns, opportunities for ophthalmic surgeons to use corneal autografts are very rare.

Clinical Report

An unemployed dock labourer aged 50 years was referred to the Corneo-Plastic Unit at East Grinstead on May 11, 1954, by Mr. S. S. Sumner of Preston.

Up to 1944 the vision had been normal in each eye, but suddenly the vision of the left eye was lost after a period of "soreness"; no active treatment was sought at the time. In 1952 the right eye became ulcerated, resulting in a scar and almost total blindness. Mr. Sumner diagnosed disciform keratitis and, when the eye was quiet, a lamellar graft was performed which gave some improvement.

The previous history revealed nothing of ophthalmic significance. The patient had been generally fit, well, and free from illnesss. He had received a blow on the top of the head with a hammer in 1946 and scalp stitches were inserted; there had been no effect on vision.

The family history revealed nothing of ophthalmic significance.

Examination (9.7.54).—The patient fixes with the right eye and the left eye is 5° divergent.

Visual acuity in the right eye is "gross hand movements" with brisk and accurate projection to a dull light; unable to distinguish fingers at 1 metre. Normal tension on palpation.

* Received for publication March 4, 1957.

A dense white scar involved almost the entire corneal area; in the centre of the scar was a 7-mm. circular lamellar graft through which could be seen scar tissue in the posterior half of the corneal thickness (Fig. 1).

FIG. 1.—Before operation. The lamellar graft and leucoma are seen on the right cornea. The left cornea is normal.

The thickness of the cornea was increased by 50 per cent. and there was deep and active vascularization throughout the scar tissue. The limbal area was clear and iris details could be seen; pupillary reactions were normal. On full mydriasis there were posterior synechiae at 12 and 1 o'clock; the lens was clear. A good red reflex was present but no fundus details could be seen.

The left eye was 5° divergent with full movements. Normal tension on palpation. No perception of light. The cornea was normal with no cells on the post-corneal surface and no scar. The anterior chamber deepened to the pupil which had a total ring synechia. There was a secondary cataract; no red reflex was discernible.

Plan of Operation.—Contralateral corneal transplantation, using the left cornea as donor to the right eye.

Operation (3.8.54).—Anaesthesia comprised surface instillation of 4 per cent. cocaine drops with a regional orbital block of 1 per cent. lignocaine. Facial akinesia was obtained by the O'Connor method and the area of the superior rectus muscle was also infiltrated.

Corneal overlay sutures were prepared on both sides; a 6-mm. full thickness donor graft was cut from the normal left cornea and with the same trephine a similar disc was cut from the scar tissue of the right cornea; after transposition the grafts were held in place by three overlay sutures. On the right side there was good apposition and contour with speedy reconstitution of the anterior chamber, but on the left side egg membrane had to be used as there was some difficulty in fitting a piece of scar tissue into a normal cornea. 1 per cent. chloramphenicol ointment was inserted, both lower lids were drawn up, and double pads applied.

First Dressing (9.8.54).—There was no lid oedema and the lid sutures were in good position; they were removed. The cruciate overlay sutures were in place on both sides and there was no disturbance of the egg membrane on the left side. All were removed; both anterior chambers were normal. No unusual vascularization or reaction; no anterior iris adhesions (Fig. 2).

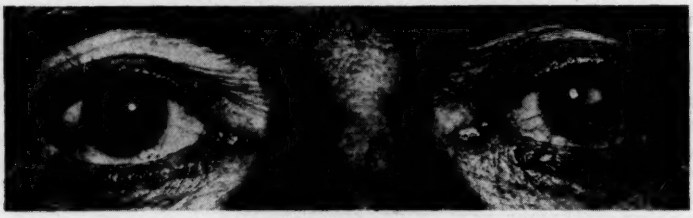


FIG. 2.—After operation, showing transposition of grafts.

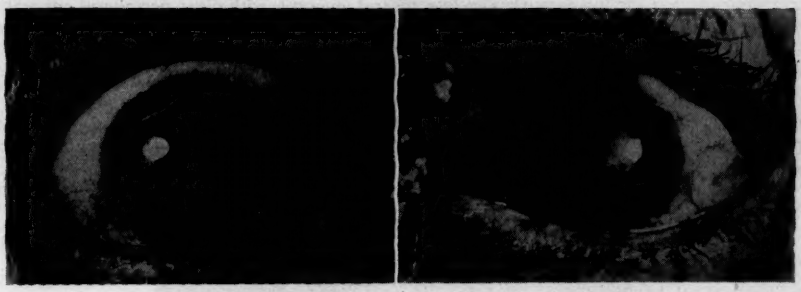
Discharge (28.8.54).—In the right eye the graft is clearing steadily and there is good fibrous ring formation. Visual acuity 6/36. No anterior synechiae. Tension normal.

In the left eye the scar disc in the cornea shows slight superficial vascularization Tension normal.

Result.—As was to be expected there were few biological changes in this autoplast graft and convalescence was uneventful.

On 7.2.57 the visual acuity in the right eye was 6/9 (unaided), and there had been no discomfort in the last 2½ years (Fig. 3*a*, *b*).

The graft in the right eye (3a) is still quite clear without vascularization and there are no complications. In the left eye (3*b*) the disc of scar tissue has healed well; it will be interesting to observe changes in this graft during the next few years.



(*a*) (*b*)

FIG. 3 (*a* and *b*).—2½ years after operation; visual acuity in the right eye = 6/9.

Case 2, Use of Donor Graft preserved at −79° C. for Full-Thickness Keratoplasty. —For some years it has been obvious that a long-term method of storing corneal donor material would be desirable when supplies improved. As a result of the Corneal Grafting Act, 1952, the supplies of donor eyes have increased at East Grinstead from 37 eyes in 1951 to 212 eyes in 1956. The method of Bürki (1947) of storage in oil at 4° C. is safely valuable up to 14 days, but, although clear optical grafts have been obtained after 23 days' storage by this method (Rycroft, 1955), such a long period of storage is not to be recommended. Unfortunately, the oil medium has the disadvantage that antibiotics in it cannot be brought into intimate contact with the donor material and also that the oil tends to cling to the corneal material at operation.

Following the promising work of Polge, Parkes, and Smith (1949) on the preservation of spermatozoa at low temperatures, it was decided three years ago with the co-operation of R. E. Billingham of University College, to try to bank eyes and corneae at −79° C. after previous treatment with antibiotics and 15 per cent. glycerol.

First the cadaver eyes or corneae were carefully examined and cultured; next, they were soaked for 20 minutes in an antibiotic solution of penicillin and streptomycin; they were then immersed for one hour in 15 per cent. glycerol. Thereafter, the material was slowly frozen to −79° C. and was maintained at that temperature indefinitely by dry CO_2 snow. When required the eyes were thawed rapidly to +37° C. and used immediately. With various modifications, and using the new medium described by Sachs (1957) instead of oil, this procedure is now in constant use at East Grinstead.

The following case was treated over 3 years ago with a corneal graft preserved in this fashion: vision has been maintained.

Clinical Report

A grinder of silica fire bricks, aged 51, complained of bad sight in both eyes, the right eye being the worse.

After diphtheria at age 2 he had had severe eye ulceration and blindness. Two operations were performed by Treacher Collins (optical iridectomies).

The patient had cement dermatitis but no other general illness.

The family history revealed nothing of ophthalmic significance.

Examination (11.11.53).—Both eyes fixed and there was no deviation.

In the right eye there was a dense white central leucoma with clear peripheral corneal tissue (Fig. 4). The anterior chamber and iris details could be seen through the periphery; there was an optical iridectomy above. The leucoma involved all thicknesses of the cornea which was increased in thickness by +25 per cent. There was no active vascularization but early appearances of band-shaped keratopathy were seen. On mydriasis the lens was clear: there was a bright red reflex but fundus details were not seen. The visual acuity was counting fingers at 1 metre. Projection was accurate and brisk to a dull light. Tension on palpation was normal.

FIG. 4.—Before operation (November 11, 1953).

In the left eye the leucoma was grey and not as dense as on the right side (Fig. 4). The cornea was of normal thickness without active vascularization. Iris details could be seen; there was a vertical optical iridectomy. On mydriasis the lens was clear and fundus details were just discernible. The visual acuity was counting fingers, but rather better than on the right side. Tension was normal on palpation. Binocular vision was just 1/60 and there was no improvement on contact lens trial.

Plan of Operation.—Full-thickness keratoplasty in the right eye.

Operation (17.11.53).—Anaesthesia included general basal sedation and local 4 per cent. cocaine drops; regional orbital block with 1 per cent. lignocaine and 5 per cent alcohol. O'Connor facial block was used with superior rectus infiltration with 1 per cent. lignocaine. Alcohol was included in the orbital and facial blocks as the patient was particularly sensitive and apprehensive.

A 5·1-mm. full-thickness keratoplasty was performed on the right eye. Fixation technique was by three overlay mattress sutures and egg membrane cover. There were no incidents or operative complications. The donor graft came from a cadaver eye excised 4 hours *post mortem* and preserved at −79° C. for 4 weeks. On inspection the donor cornea was clear and bright with no wrinkles or air bubbles after thawing.

First Dressing (24.11.53).—The graft had a good contour; there was wrinkling of

Descemet's membrane. The anterior chamber had reformed and iris details could just be seen through the graft. There were no iris adhesions and no undue reactions. The sutures were removed and a uniocular pressure dressing applied.

Three days later there was considerable general psychiatric disturbance, but no damage was done to the eye.

Discharge (8.1.54).—There were many patches of eczema on the face, neck, and hands, which was considered to be associated with the nervous condition, the patient having had similar skin reactions before. The right eye was white and quiet but the graft was now hazy. The contour was good and the fibrous ring was well healed (Fig. 5) with a small shelf in the infero-nasal quadrant. There was no vascularization and no epithelial bullae were present; the ocular tension was normal.

FIG. 5.—7 weeks after operation. There is no vascularization but the graft is completely cloudy. A fresh graft at this period would have been clear.

Result.—The graft and adjacent tissue continued to clear slowly; there was no active superficial or deep vascularization, the visual acuity was 6/36 (Fig. 6, 25.4.55).

FIG. 6.—17 months after operation (April 25, 1955). The graft is clearer and the optical iridectomy is seen. There is even contour with a good fibrous ring.

Approximately 2 years after the operation (28.10.55), the graft was 100 per cent. clear and iris details were well seen (Fig. 7*a* and *b*, opposite). Placido keratoscopy showed even and regular circles. Visual acuity without correction was 6/24 to 6/18 (1 letter). Fundus details were well seen and were normal.

(a)

(b)

FIG. 7 (*a* and *b*).—Nearly 2 years after operation (October 28, 1955). The graft is clear and the visual acuity is 6/12 (unaided).

The eye was quiet with normal tension 3½ months later. The visual acuity was 6/12 (unaided) and N.10.

Comment.—This case shows the use of a donor graft preserved for a month at −79° C., and establishes *prima facie* evidence that long-term storage at low temperature is possible. It is noted that the graft behaved in a different manner from a graft used after short-term preservation at +4° C.; there was a long latent period before function was restored. This delay in the recovery of function has also been noted in ovary transplantations when the material has been preserved by this method. More recent corneal graft cases, however, with modification of deep freeze technique, have given very encouraging results, and it is felt that this method will become the bank method of preservation for the future.

Case 3, Severe Corneal Damage and Multiple Perforations treated by Lamellar Keratoplasty with Recovery of Useful Vision.—This illustrates the progress of a man who was quite blind, and whose case would have been considered hopeless a few years ago; after several operations there was restoration of corrected vision to 6/12. It also emphasizes how a very small area of clear cornea can be of immense value to a patient if he has the courage to face many operations and the will to persevere in rehabilitation.

Clinical Report

A research fellow in chemistry, aged 26, was studying in Paris, when on May 15, 1950, whilst he was purifying an ethyl compound, a glass retort exploded. He was treated for multiple eye perforations in Paris and subsequently returned to England, where Mr. Roy Thomas referred him to East Grinstead (Fig. 8, opposite).

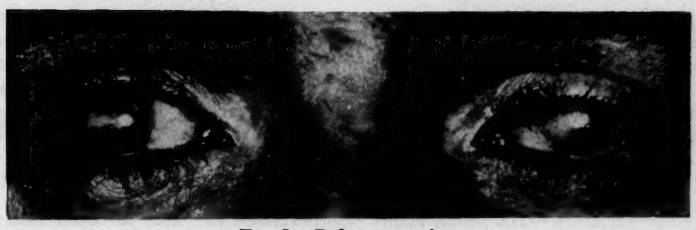


FIG. 8.—Before operation.

Examination (9.10.50).—The right cornea showed many circular grey opacities; some were discrete and some were confluent. These opacities marked the sites of multiple perforations of the cornea by spicules of glass; they involved total corneal thickness. Many fine glass particles were also embedded in the stroma of the cornea and iris. Through the edge of the nasal cornea many anterior synechiae were visible and there were lens capsule remnants; a dim red reflex with no details could just be detected. The visual acuity was "perception of gross hand movements but inability to see fingers"; there was brisk and accurate projection to a dull light in all quadrants. The ocular tension was normal on palpation.

The left eye showed a similar condition with more confluence of the opacities and few anterior chamber details could be seen. Vision was "perception of light with no accurate projection", and the ocular tension was subnormal on palpation.

There was nothing of significance in the past ophthalmic, general, or social history; spectacles had not been worn and vision had been normal and equal in each eye. There had been no previous eye operations (Fig. 9).

FIG. 9.—Right eye, showing multiple healed corneal perforations.

Plan of Operation.—As the right eye was aphakic, it was considered that a full-thickness graft was not justified, especially as this was the only eye with potential sight. It was decided that attempts should first be made to clear the anterior synechiae and then to carry out a deep lamellar keratoplasty. The left eye was beyond treatment.

Operations (7.11.50).—Anterior synechiotomy (3 synechiae) followed by subconjunctival mydricaine.

Two weeks later the patient suffered from otitis media with perforation of the right ear drum as a result of the previous explosion; he had 30 per cent. loss of hearing.

(12.12.50).—Second anterior synechiotomy (2 synechiae divided). The central area of the cornea was now free from iris adhesions.

(9.2.51).—Lamellar keratoplasty. A 7·1-mm. graft bed was prepared, going as deeply

as possible; several glass spicules were encountered on the way. A lamellar graft of the same size, which had been taken 15 hours after death and stored for 2 days, was inserted. Fixation was by egg membrane and overlay silk sutures. Through the graft bed it was possible to see anterior chamber details in the upper and inner quadrant, and gross peripheral anterior synechiae were seen underneath dense scar tissue on the temporal side. Convalescence was uneventful but there was considerable superficial trunk vascularization.
(9.4.51).—Strip peritomy with cauterization and dissection—excision of trunk vessels.

Discharge (22.4.51).—The visual acuity was described as "able to count fingers and to get about; a guide stick is no longer necessary" (Fig. 10).

FIG. 10.—Right eye after lamellar keratoplasty, showing small clear areas of cornea.

(3.7.51).—The patient was referred to Mr. J. Pike of Messrs. Rayner for investigation of visual aids. The graft was clear and through it could be seen anterior chamber details and two anterior synechiae; there was also a capsule anterior synechia. Mr. Pike was able to obtain 6/18 with a prism glass and J.3 with the addition of a collimating lens.
(2.1.53).—Visual acuity in the right eye with correction was 6/12 and J.8.

Result.—This patient subsequently returned to his studies at the Sorbonne and graduated as a doctor of philosophy.
(9.12.55). Visual acuity with a contact lens (Mr. F. Ridley) was 6/60, which could be improved to 6/18 with a telescopic lens.
(21.12.56) The patient was now an extra-mural lecturer in science. He had abandoned the contact lens as his corrected visual acuity was 6/18, and J.8 was obtained with telescopic correction. There was almost complete adaptation and the patient went about quite freely by himself.

The results in these cases would not have been possible without the able co-operation of my colleagues, G. Romanes and M. Garber, at East Grinstead. Sister C. King and her assistants were responsible for the skilled nursing which is so essential in corneal graft cases. I am indebted for the photographs to Mr. Gordon Clemetson of the Photographic Unit.

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OPTIC NERVE TUMOUR TREATED BY KRONLEIN'S LATERAL ORBITOTOMY*

BY

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Case Report

A boy aged 12 complained of pain in the left eye on July 27, 1955, when the visual acuity in each eye was reported to be 6/6. On August 26, 1955, the visual acuity in the right eye was still 6/6, but that in the left eye was reduced to 6/12, and there was noticeable left-sided exophthalmos. On January 4, 1956, the left eye was blind and the proptosis had markedly increased. *X* rays showed the left optic foramen to be enlarged and a diagnosis of glioma of the optic nerve was made in Calcutta.

The boy was examined by me for the first time on September 26, 1956, when the findings and diagnosis were confirmed. There was a marked proptosis on the left side, the eyeball being displaced downwards and inwards (Fig. 1). The ocular movements were restricted upwards and outwards. The left fundus showed optic atrophy, the papilla was swollen, and the vessels were engorged and tortuous. On and around the disc a few abnormal vessels were seen.

Operation.—Kronlein's lateral orbitotomy was performed by me on October 8, 1956. The presence of an optic nerve tumour was confirmed and this was excised *in toto*. Only one complication was encountered; the bony fragment was fractured while being removed.

The post-operative recovery, except for an irregularly febrile course for the first 4 days, was uneventful.

Result.—Fundus examination 4 days after the operation showed a completely ischaemic retina. On the tenth day adduction was normal, abduction was absent, and elevation and depression of the globe were restricted. At the time of discharge on October 29, 1956, there was a slight ptosis of the left upper lid and a convergent squint of the lef eye. The proptosis had decreased by 10 mm. (Fig. 2).

FIG. 1.—Appearance of the patient before Kronlein's operation.

FIG. 2.—Appearance at the time of discharge 3 weeks later.

* Received for publication June 29, 1957.

Histopathological Examination.—Macroscopically the excised mass (Fig. 3) showed a totally neoplastic optic nerve with intact sheaths and necrosis at its posterior end, its diameter being 0·8 mm.

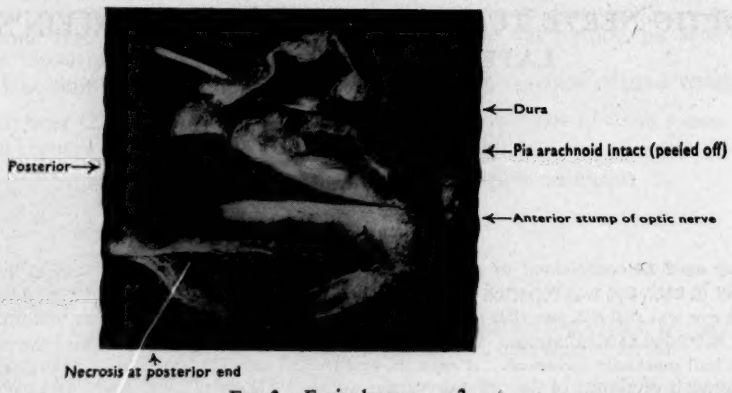

FIG. 3.—Excised mass. ×3.

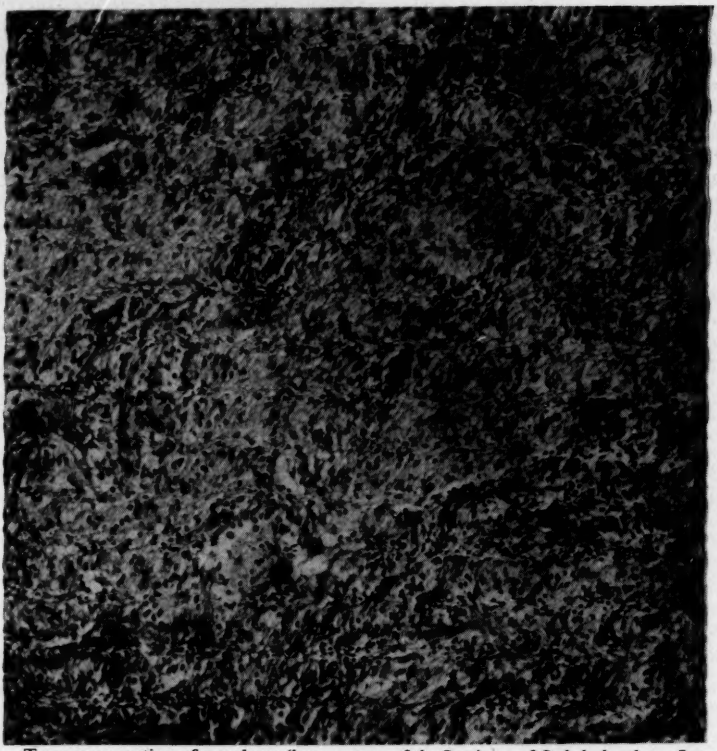

FIG. 4.—Transverse section of neoplasm (by courtesy of the Institute of Ophthalmology, London).

A section was submitted for microscopical examination to Dr. N. Ashton of the Institute of Ophthalmology, London, who made the following report:

The section submitted for examination is stained with haematoxylin and eosin, and shows a portion of optic nerve in which the septa are distorted and widely separated by proliferating masses of glial cells with pale round or oval nuclei and well-marked cytoplasmic vacuoles. They lie in a dense stroma of delicate fibres, and in some areas surround irregular spaces containing hyaline eosinophilic transudate. The histological picture is typical of glioma of the optic nerve (Fig. 4).

Follow up (June 17, 1957).—The result was excellent in the primary position; there is no ptosis (Fig. 5), normal adduction (Fig. 6), and normal depression (Fig. 7). Defective elevation (Fig. 8) and restricted abduction (Fig. 9) are the only delayed sequelæ of this operation.

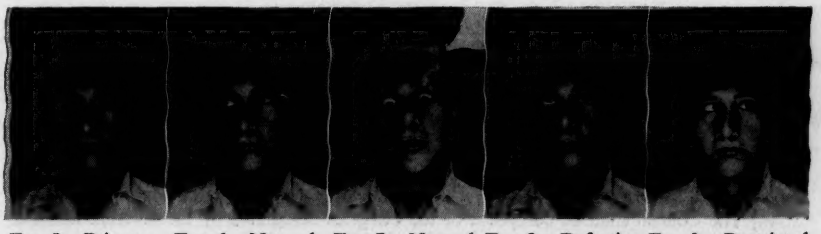

FIG. 5.—Primary position

FIG. 6.—Normal adduction

FIG. 7.—Normal depression

FIG. 8.—Defective elevation of left eye

FIG. 9.—Restricted abduction of left eye

The left eye is slightly enophthalmic, and the size of each pupil, despite total blindness on the left side, is 3 mm. The left pupil does not react at all.

Summary

A case is reported of oligodendroglioma of the optic nerve, successfully treated by Kronlein's operation.

My thanks are due to Dr. Norman Ashton, Director of Pathology, Institute of Ophthalmology, London, for histopathological report and the photomicrograph.

Brit. J. Ophthal. (1957) **41**, 770.

NOTES

European Ophthalmological Society

Delegates from the European countries met at the old *Medical Faculty in Paris*, under the presidency of Dr. P. Bailliart, on May 14, 1957, with the object of forming a European Ophthalmological Society.

The Secretary General stated that he had received as members all European countries except Hungary, Poland, and Roumania, who were in agreement in principle, but who had not sent a delegate and that Bulgaria and Russia had not yet given an answer.

Statutes.—The following statutes were unanimously agreed:

(1) The European *Ophthalmological Society* is founded. (Societas Ophthalmologica Europaea.)

(2) It shall be directed by a *Board of three members*, and a Council composed of the national delegates.

(3) The three members of the Board, whose functions are to be international in character, are as follows:

President:	Doctor Paul Bailliart (*Paris*)
Secretary General:	Professor Jules François (*Ghent*)
Treasurer:	Professor A. Franceschetti (*Geneva*)

The President shall be replaced every 4 years by an elected member of a different nationality.

(4) The Council shall be composed of the delegates designated by the different national Societies:

Prof. R. Thiel (*Germany*), Prof. J. Böck (*Austria*), Prof. L. Coppez (*Belgium*), Dr. P. Ladekarl (*Denmark*), Dr. H. Arruga (*Spain*), Prof. M. Vannas (*Finland*), Dr. J. Sédan (*France*), Mr. F. W. Law (*Great Britain*), Prof. J. Charamis (*Greece*), Prof. A. Hagedoorn (*Holland*), Dr. L. E. Werner (*Ireland*), Prof. L. Maggiore (*Italy*), Dr. P. Riise (*Norway*), Prof. Lopes de Andrade (*Portugal*), Prof. G. von Bahr (*Sweden*), Prof. M. Amsler (*Switzerland*), Prof. V. Vejdovsky (*Czechoslovakia*), Dr. N. Ayberk (*Turkey*), Prof. Zv. Pavisic (*Yugoslavia*).

Additional council members may be co-opted.

(5) Ophthalmologists of European nationality shall have the right to become members of the European Ophthalmological Society on request, provided they are members of their national Society.

(6) Ophthalmologists from other continents may be admitted as "associate members" when introduced as such by the Council.

(7) The European Ophthalmological Society shall present an account of its foundation to the International Council and will request representation *ex officio*.

(8) The European Ophthalmological Society shall organize a Congress every 4 years, alternating with the World Congress at 2-year intervals.

(9) All the languages of the countries represented in the European Ophthalmological Society may be used at Congresses. The administrative languages shall be designated by the Council before each Congress.

(10) Subscriptions to the European Ophthalmological Society are to be paid every 4 years on the occasion of the Congress. The Society is entitled to accept gifts and grants.

(11) The Board is qualified to call meetings of the Council whenever this is considered necessary. The advice of Council members may be given by correspondence.

The following decisions were also taken:

(1) The non-European foundation members of the old "Société Latine d'Ophtalmologie"

have been declared honorary members of the European Society:

Prof. R. Argañaraz (*Buenos Aires*), Prof. C. Espildora Luque (*Santiago*), Dr. H. Ferrer ((*Havana*), Prof. J. Malbran (*Buenos Aires*), Dr. J. Vidal (*Rio de Janeiro*). The Secretary General of the old Société Latine d'Ophtalmologie, Prof. E. Filippi-Gabardi (*Bologna*), is nominated honorary secretary general.

(2) The first Congress of the European Ophthalmological Society is to be held in Athens in April, 1960.

(3) The administrative languages for next Congress will be: French, English, and German. Invitations in Spanish will be sent to South America.

(4) The subject of the next Congress will be: Secondary Glaucoma. There will be no free communications.

(5) Registration fees at the Congress will be of $25 (exchange value in dragmes) for titulary members, and of $12 (exchange value in dragmes) for associate members.

(6) The European Ophthalmological Society will send its secretary general as delegate to the centenary meeting of the German Ophthalmological Society (*Heidelberg, September, 1957*) and to the fiftieth anniversary meeting of the Swiss Ophthalmological Society, *Zürich*, September, 1957).

(7) The next meeting of the Council of the European Ophthalmological Society will be held during the International Congress in Brussels in 1958.

The Secretary General,
PROF. J. FRANÇOIS.

IRISH OPHTHALMOLOGICAL SOCIETY

Annual Meeting, 1957

The annual meeting of the Irish Ophthalmological Society was held in Dublin jointly with the Society of British Neurological Surgeons on May 16–18, 1957, under the chairmanship of their respective presidents, Dr. Alan Mooney and Mr. W. R. Henderson.

In his opening paper on "Some Neuro-ophthalmological Problems", Dr. Mooney discussed the changes in vision, visual fields, and optic disc appearances in some 22 cases which presented problems of diagnosis and treatment mainly in intracranial disease.

Dr. Max Chamlin (*New York*), in a paper on "Visual Field Changes produced by X-ray Treatment of Pituitary Tumours", selected forty out of 180 cases to describe the course of improvement in the visual fields subsequent to irradiation. Improvement may occur, 2, 3, or even 4 years after treatment. He advocated using $1^{mm}/2000$ and $2^{mm}/330$ targets.

The technique of orbital angiography, including the injection of contrast medium into the angular vein, was described by Professor Krayenbuhl (*Zürich*).

Dr. Uihlein (*Mayo Clinic, Rochester, Minn.*), speaking on "Acute Visual Failure as a Neurosurgical Emergency", discussed the aetiology of visual failure, the order of frequency in his experience being pituitary tumour, optic nerve tumour, supraclinoid aneurysm, parasellar lesion, carotid arterial thrombosis, and third ventricle hydrocephalus.

A symposium on the "Blood Supply of the Chiasma and Optic Nerves in relation to Visual Field Defects", was opened by Professor François (*Ghent*). Professor Erskine (*Dublin*) followed with a discussion on the perivascular neuroglia, using the new technique of phase-contrast/colour-contrast microscopy. Professor Brodie Hughes (*Birmingham*) spoke on the clinical implications of this subject.

Papers were also presented by Mr. Roper-Hall (*Birmingham*) on "Optic Disc Oedema without Raised Intracranial Pressure" and Professor G. I. Scott (*Edinburgh*) on "The Ocular Aspects of Endocrine Exophthalmos".

Dr. Frank Walsh (*Baltimore*) gave the Montgomery Lecture on "Third Nerve Re-

generation: Clinical Evaluation". He described the apparent palsies which occur, the superior and inferior recti counteracting one another and the eye turning inwards. Electromyography had been helpful in revealing the activity of the individual muscles concerned. In third nerve palsy due to diabetes, the lesion was probably the result of demyelination and subsequent recovery was often noted.

At the final session the two societies met separately. Ophthalmological papers were given by Dr. MacDougald (*Dublin*) on "The Detection of Glaucoma", Mr. H. B. Stallard (*London*) on "Anterior Flap Sclerectomy with Basal Iridectomy", Sir Luigi Preziosi (*Malta*) on "Flap and Filtration in Preziosi's Operation", and Dr. F. McAuley (*Dublin*) on "Technique and Results of Retinal Detachment Surgery using Binocular Indirect Ophthalmoscopy".

The success of the meeting was further increased by the warm welcome and hospitality from our colleagues in Dublin.

National Council to Combat Blindness

The Scientific Advisory Committee of the National Council to Combat Blindness announces that it is now accepting applications for its 1958/59 FIGHT FOR SIGHT grants-in-aid, research fellowships, and summer (1958) student fellowships. In accordance with its programme of financing research in ophthalmology and related sciences and encouraging qualified investigators to further research, the Scientific Advisory Committee will consider all applications at its ninth annual meeting in June, 1958.

The closing date for receipt of completed applications for grants and fellowships has been advanced to March 1, 1958, in order to allow time for processing and review. Applications for summer student fellowships will be reviewed in advance of the June meeting.

Appropriate forms may be obtained from the Secretary, National Council to Combat Blindness, Inc., at the Council's new address: 41 West 57th Street, New York 19, N.Y.

Muslim University, Aligarh, India

Institute of Ophthalmology

Professor Tulsi Dass, F.R.C.S., lately Professor of Ophthalmology at Amritsar has become Director of the Institute of Ophthalmology, Aligarh, India.

Dr. F. C. Rodger of the United Kingdom has joined the Aligarh Institute of Ophthalmology as Research Professor under the Colombo plan.

The Ross Foundation

A generous contribution was made from the Ross Foundation towards the expense of the numerous illustrations in the paper "The Eye in Vascular Disease" by Robert Leishman.

It is regretted that this acknowledgement was omitted from the issue in which the paper appeared (November, 1957).

ED.

OPHTHALMOLOGIST wanted in Eastern Canada as assistant to busy specialist. Considerable amount of operative work. Some knowledge of E.N.T. an advantage. Excellent prospects for advancement. Salary first year $9,000. Principal will be in U.K. in Spring for personal interviews. Write (giving experience, age, marital status, religion, and snapshot) to Box No. 70, *British Journal of Ophthalmology*, B.M.A. House, Tavistock Square, London, W.C. 1.

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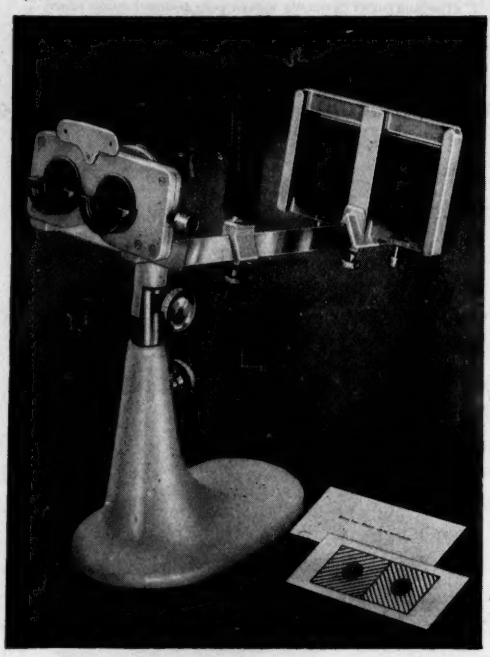

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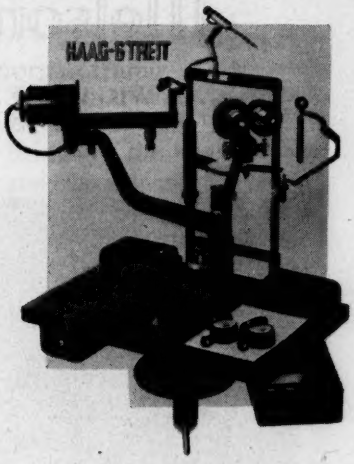

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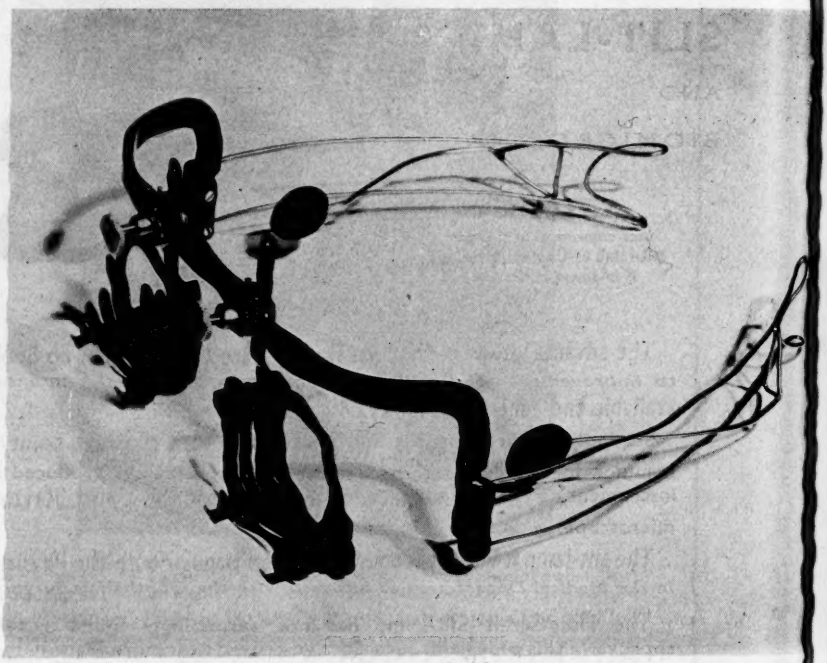

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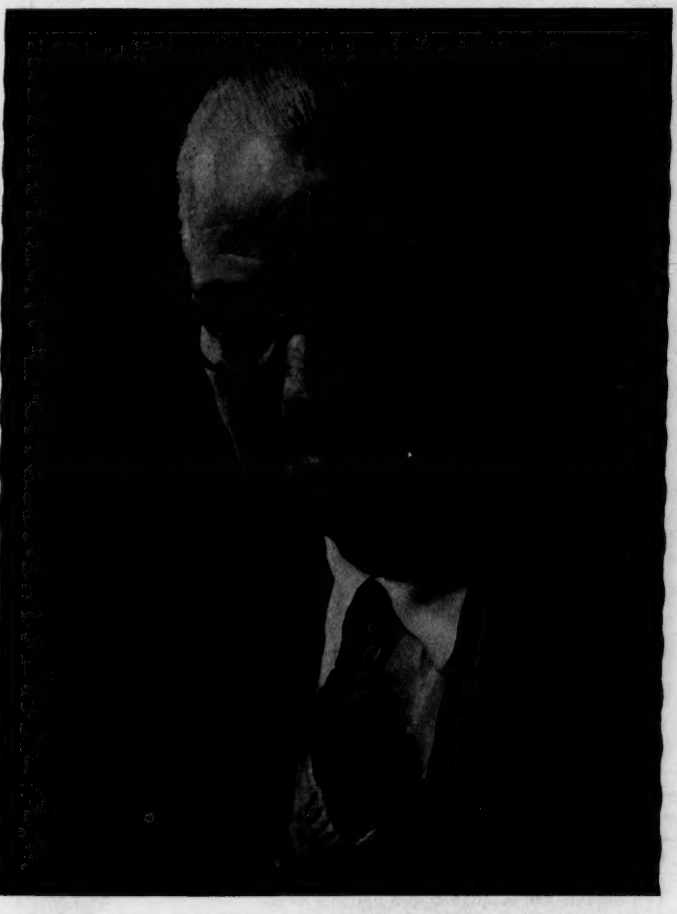

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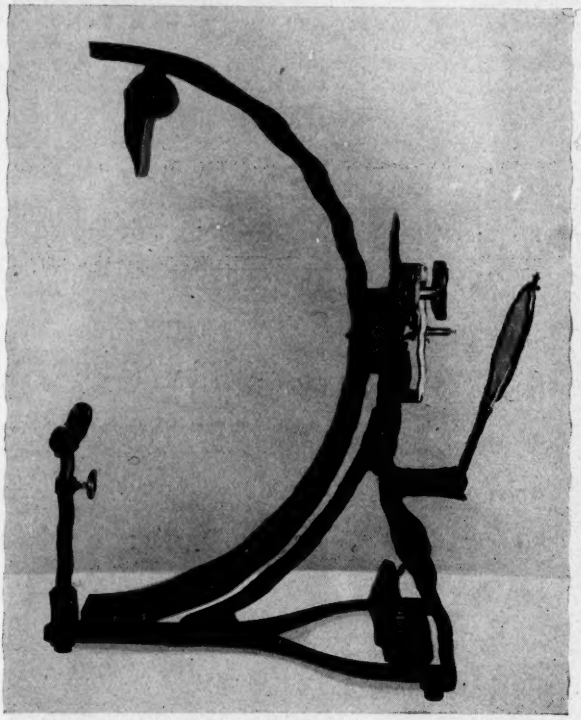

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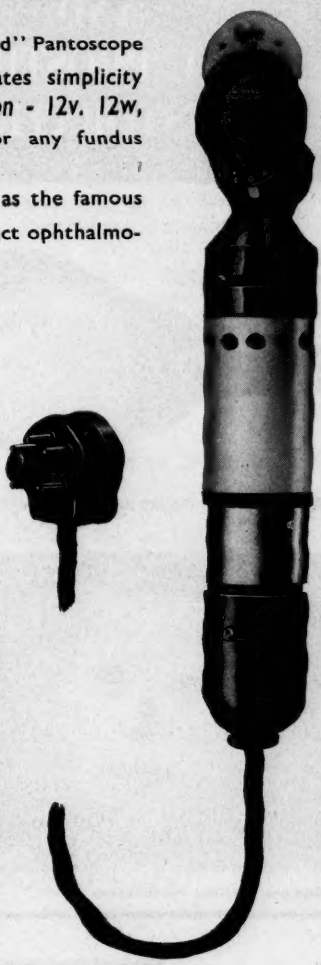

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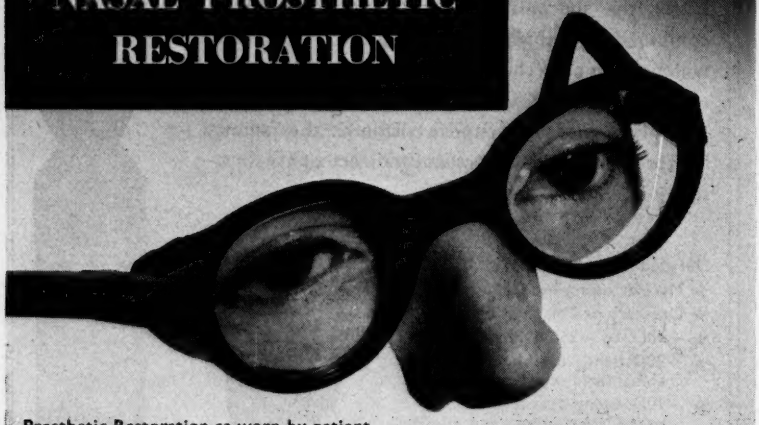

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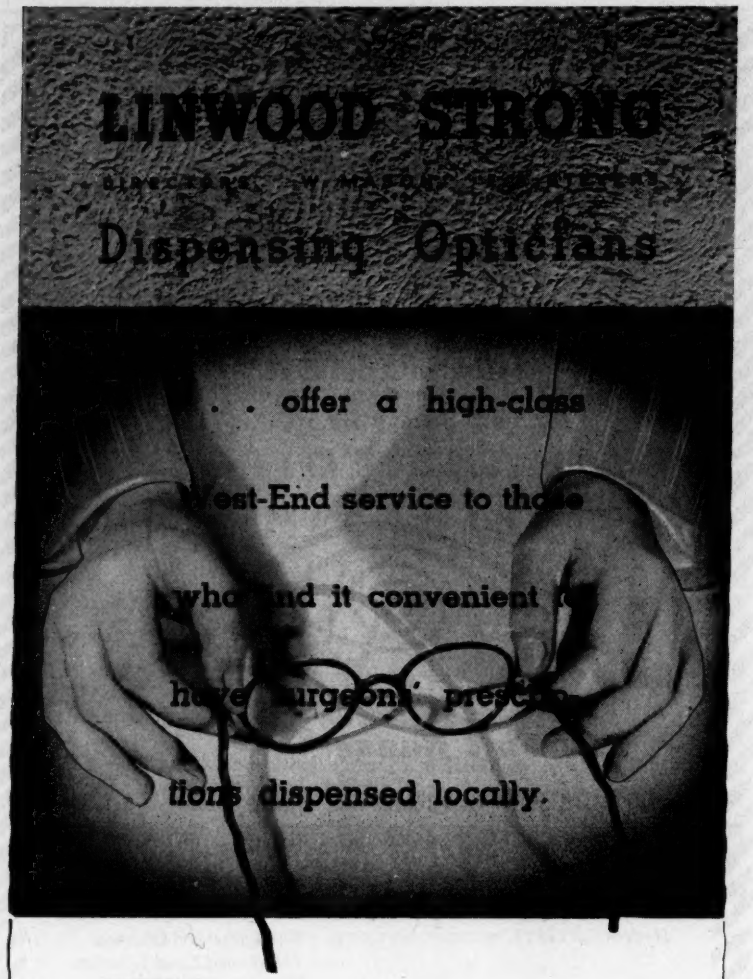

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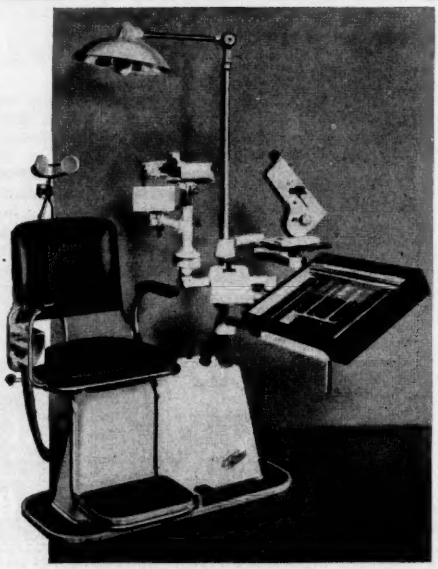

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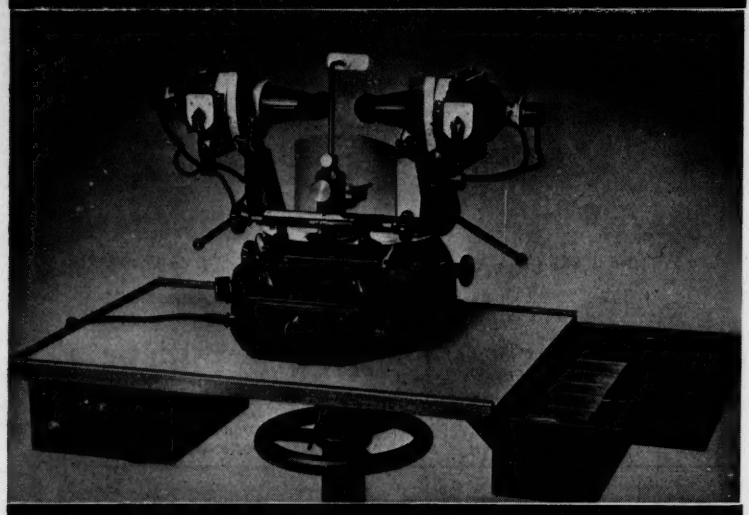

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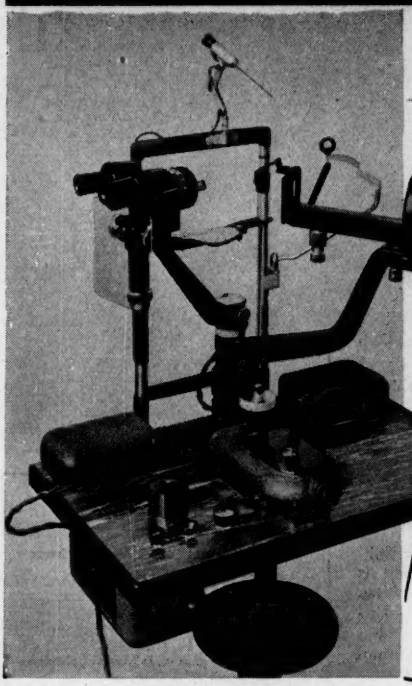

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0.25 to 3.00 *in steps of 0.25 Dioptres.*
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8 Prisms — ¼, 1, 1, 2, 3, 4, 6, 8.

9 Accessories:
Maddox Rod.
Red & Green Glass.
2 Cross Lines.
Occluder Disc.
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TOTAL Number of Lenses — 225

Our Standard Trial Case now contains our major range of small aperture trial lenses fitted in a solidly made panelled, lift-off lid case with removable tray. The lid is secured by 2 strong spring clasps and a lock and key is provided. Can be supplied in natural mahogany or oak.

The lenses are well spaced for easy removal. The indices are clearly engraved on white plastic with black figures. Outside measurements 21½" × 15¾" × 2¾".

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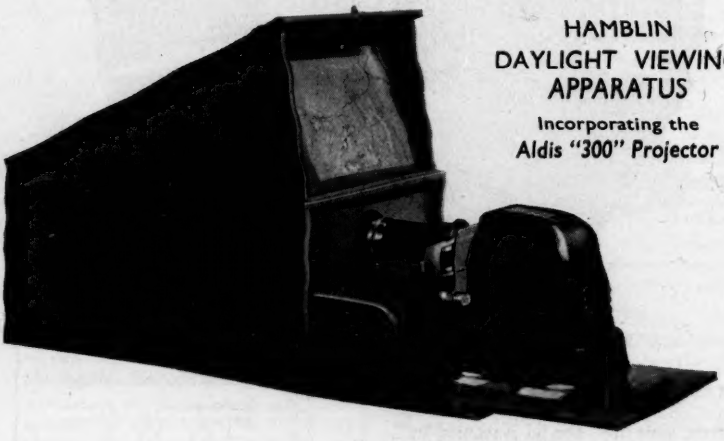
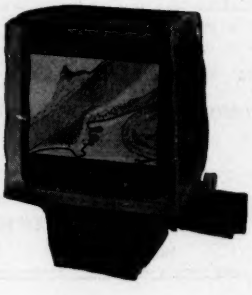


HAMBLIN
DAYLIGHT VIEWING
APPARATUS

Incorporating the
Aldis "300" Projector

When it is inconvenient to darken an Outpatient Department for teaching purposes, Hamblin Miniature Slides may be admirably demonstrated by means of this back-projection equipment. Set on a table beside the surgeon, its special screen is very well placed for him to point out notable features of the pictures which he projects. Out of use, the device is closed to form its own carrying case, containing and protecting the lantern and set of slides.

The size of picture, about 12 inches by 8 inches, is well suited to tutorial groups of up to twenty or so. For formal lectures, the Aldis "300" projector employed separately, will throw pictures nearly 4 ft wide on a conventional screen.



"VISTAVU" SLIDE VIEWER

Miniature slides appear on the screen of this compact daylight viewer as brightly illuminated images, approximately 8 inches by 5½ inches, a size adequate for small groups.

HAMBLIN MINIATURE LANTERN SLIDES

For teaching small groups and for informal lectures, miniature slides, 5 cms. square, are ideal. Hamblin Miniature Lantern Slides, mostly in full colour are available in a range of typical fundus and external ocular appearances especially selected for teaching. The slides available are enumerated below.

The slides are photographic reproductions of master paintings made under the guidance of ophthalmologists. Special slides, to individual requirements, can be made to order.

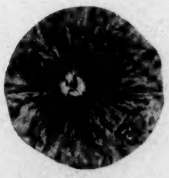
A selection of lantern slides of standard size (3¼ ins. square) is also available.

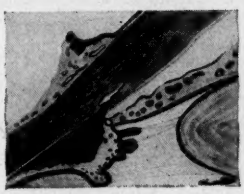
FUNDUS

Miniature No.	Condition.
MF 1.	Blonde Fundus.
MF 3.	Medium British Fundus
MF 2.	Tigroid Fundus.
M4 4.	Negro Fundus.
MF 5.	Physiological Cupping.
MF 6.	Myopic Atrophy of Choroid.
MF 7.	Opaque Nerve Fibres.
MF 8.	Pseudo-Papilloedema.
MF 9.	Glaucomatous Cupping.
MF 10.	Primary Optic Atrophy.
MF 11.	Secondary „ „
MF 12.	Retinitis Pigmentosa.
MF 13.	Papilloedema.
MF 14.	Myopic Detachment.
MF 15.	Melanomatous Detachment.
MF 16.	Haematogenous Haemorrhages.
MF 17.	Embolism of Central Artery.
MF 18.	Thrombosis of Central Vein.
MF 19.	Acute Choroiditis.
MF 20.	(Tays) Colloid Deposits at Macula.
MF 21.	Old Choroiditis.
MF 22.	Diabetic Retinitis.
MF 23.	Albuminuric Retinitis.
MF 24.	Advanced Arterio-sclerosis.
MF 25.	Miliary Tuberculosis.
MF 26.	Diabetic Lipaemia.
MF 27.	Albinotic Fundus.
MF 28.	Rupture of the Choroid.

The John Foster Comparative Pictures of Fundus Changes of General Diagnostic Significance.

Miniature No.	Condition.
MF 29.	Normal Abnormalities.
MF 30.	Pigmentary Variations.
MF 31.	Disc Changes.
MF 32.	Haemorrhages.
MF 33.	Detachments, Choroiditis
MF 34.	Disc Changes.
MF 35.	Disc Changes.





The above illustrations are full size.

Other slides will be added from time to time.

EXTERNAL APPEARANCES

Miniature No.	Condition.
ME 1.	Rosacea Keratitis.
ME 2.	Amaurosis from Glioma.
ME 3.	Angular Conjunctivitis.
ME 4.	Blepharitis.
ME 5.	Cuneiform Cataract.
ME 6.	Congenital Lamellar Cataract.
ME 7.	Chalazion.
ME 8.	Ophthalmic Neonatorum.
ME 9.	Dendritic Ulcer.
ME 10.	Phlyctenular Ulcer.
ME 11.	Hypopyon Ulcer.
ME 12.	Prolapse of Iris (traumatic)
ME 13.	Cyclitis, K.P., occlusio.
ME 14.	Dacryocystitis, acute.
ME 15.	Dislocation of Lens (posterior).
ME 16.	Epicanthus.
ME 17.	Episcleritis.
ME 18.	Acute congestive glaucoma.
ME 19.	Interstitial Keratitis.
ME 20.	Pterygium.
ME 21.	Ectropion.
ME 22.	Entropion and Trichiasis.
ME 23.	Trachoma.
ME 24.	Spring Catarrh.
ME 25.	Disciform Keratitis.
ME 26.	Follicular Conjunctivitis.
ME 27.	Pinguecula.
ME 28.	Coronary Cataract.
ME 29.	Hordeolum.
MD 1.	Section through angle of anterior chamber.
ME 30.	Iritis/Glaucoma (J. Foster)
ME 31.	Concomitant and Paralytic Strabismus.
MD 2.	Tear Cycle.
	Plain Slide for drawing on.

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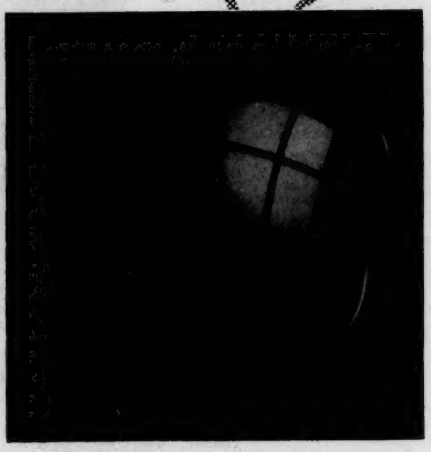

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